Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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Association of British Neurologists	Evidence Review D	058	001	The committee provide 'examples' of differential diagnosis for ME/CFS in eleven categories including neurological disorders. They have conspicuously omitted psychiatric disorders such as depression and anxiety, of which fatigue is a core symptom. The only mention of depression or anxiety as differential diagnoses in this whole diagnostic section was in relation to people misunderstanding ME/CFS (p57, line 19)	Thank you for your comment. The committee have revised the list of differential diagnosis in evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
Association of British Neurologists	Evidence Review G	General	General	The evidence review has not adopted a standard approach to synthesising the data. We are presented with over 1000 pages in Appendix G and H but with virtually no meta-analysis across main measures or looking at primary end points to allow the reader to compare trials/treatments and data. Something seems to have gone badly wrong with clinical and statistical oversight of the way in which clinical evidence is normally synthesised.	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Only studies comparing the same interventions and using the same outcome can be combined in meta-analysis. The number of studies relevant to each comparison of interventions were limited and the outcome measures reported differed, so it was not possible to combine many of them in meta-analysis.
Association of British Neurologists	Evidence Review G	006	007	The committee analysed data using 'longest follow up available' data point from trials, rather than the pre-specified endpoint for the primary outcome measures. This is inexplicable and highly problematic, because after the end of trials many patients in the control group choose to have additional treatment, reducing the power to detect a treatment effect at later time points. Whilst it is reasonable to consider the latest available data, it is unreasonable to give this greater weight than data at the pre-specified ending of the trial. The review needs to be carried out again ensuring that the pre-specified primary endpoints are considered as the key findings of randomised controlled trials.	Thank you for your comment. Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is

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				An example of how problematic this is can be seen in the PACE trial (White *et al.*, 2011) which we highlight because it is the largest RCT being considered. In this study the primary end points were at 52 weeks. After that time there was naturalistic follow up, but patients could crossover into other treatments. Yet the committee chose to look at endpoints from 134 weeks – 2 years after the end of the trial. This is not how RCTs should be evaluated as even basic trial methodologists should know.	collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline.
Association of British Neurologists	Guideline	General	General	The ABN regard ME/CFS as a serious and disabling disorder affecting the nervous system. The existing therapies for this condition are only modestly effective on average and we support efforts to develop greater understanding and treatment for this condition. We also recognise a group of patients with ME/CFS for whom current treatments are not helpful or where treatment may have been associated with deterioration. We respect all patients'	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is

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				rights to not have a treatment that is offered or decide it is not helping them. We approve of the suggestions for personalised management plans The ABN does not regard this guideline as fit for purpose or meeting the usual high standards of NICE. This response is not a request for minor changes. There are so many flaws with this document, that we would request an independent review of the process by a new committee. We suggest that there should be scrutiny by NICE of the way that the committee have gone about their task and an investigation of systematic bias and impartiality in the preparation of the guidelines. We think it would be possible to produce a guideline that satisfies patient stakeholders who are vigorously opposed to rehabilitation therapies, and yet recognises that for many patients such therapies can be helpful. Some of the key issues are: 1. The way that the evidence review has been conducted – especially in relation to case definitions excluding subjects with post-exertional malaise, inaccurate analysis of the end points of trials, and inadequate assessment of harm has meant that large amounts of good quality of evidence has been wrongfully rejected on the basis of low quality (discussed in detail below) 2. Evidence has in many places been inappropriately supplanted by the committee's own experience in a marked departure from standard NICE practice. Randomised controlled trials of complex interventions will inevitably have some limitations, but it may be not the appropriate to evaluate them according to criteria designed for drug trials(Turner-Stokes and Wade, 2020). Clinical trials, even with some limitations, provide stronger evidence than expert opinion. This guideline differs markedly from other NICE guidelines of complex disorders in the extent to which the	collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). In evidence review D-Diagnosis the committee have revised the list of differential diagnosis and added, mental health conditions: anxiety, depression or mood disorders.

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				committee's opinion has been relied on over clinical trial evidence. 3. Fatigue is a common and often core symptom of many neurological disorders such as multiple sclerosis, Parkinson's disease and neuromuscular disorders. In multiple sclerosis especially, a condition with many parallels to ME/CFS, there is a range of evidence that treatments such as cognitive behavioural therapy (CBT)(van den Akker *et al.*, 2016) and graded exercise therapy (GET)(Heine *et al.*, 2015) show modest benefit and an absence of harm for associated fatigue. We do not believe that people with ME/CFS have a mechanism of fatigue which is radically different to other neurological conditions. These guidelines would result in people with ME/CFS being excluded from the offer of treatments that have a proven evidence base in people suffering with other neurological conditions 4. The authors of the document appears to have a strong anti-psychiatry bias – especially in relation to differential diagnosis, where psychiatric disorders that have fatigue as a core feature of their diagnosis such as depression or anxiety have been completely omitted. ME/CFS and those suffering from it must be treated seriously and with respect. The ABN recognises that patients with ME/CFS have often had poor experiences of healthcare, been wrongly made to feel blamed for their condition or had their illness inappropriately attributed to entirely psychiatric factors. However, avoiding stigma in ME/CFS should not be an excuse for marginalising or stigmatising psychiatric disorder or treatments. 5. The guideline makes recommendations not to offer treatments that are current standard practice on the basis of a flawed assessment of the evidence. This would result in removing access to treatment approaches which many patients currently choose, and which are a central part of physical and psychological rehabilitation for neurological disorders.	*Fibromyalgia* Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated.

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				6. This guideline is entirely inconsistent with the 2007 ME/CFS guideline despite relying on substantially the same evidence base. 7. The guideline is also wholly inconsistent with NICE guidelines for chronic primary pain (which incorporate the condition fibromyalgia) which recommends both cognitive behavioural therapy and graded exercise. Fibromyalgia overlaps substantially diagnostically with ME/CFS (Jason *et al.*, 1999). As the authors of this guideline point out severe pain is a very common symptom in severe ME/CFS and is found at high frequency. In addition, post-exertional malaise and comorbidity of ME/CFS is very common in individuals with chronic primary pain. These guidelines are therefore mutually incompatible for practising clinicians.	
Association of British Neurologists	Guideline	General	General	The balance between committee opinion and clinical evidence in the "Rationale and Impact" section of the document is very striking. Extensive clinical trial data is barely mentioned. The committee's own experiences and opinions are mentioned on multiple occasions. NICE processes require that recommendations are based on evidence as far as possible. The impression of the ABN is that this guideline has departed from usual NICE processes in this regard. This reliance on opinion necessarily creates a risk that the guidelines could be biased by the individual opinions of committee members, in a system where the committee is not constituted to adequately represent all stakeholders and does not follow a formal "consensus" process.	Thank you for your comment. We disagree there is a reliance on individual opinion in this guideline and this has influenced the recommendations. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline.

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					The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership reflects the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Association of British Neurologists	Guideline	General	General	References van den Akker LE, Beckerman H, Collette EH, Eijssen ICJM, Dekker J, de Groot V. Effectiveness of cognitive behavioral therapy for the treatment of fatigue in patients with multiple	Thank you for these references.

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				sclerosis: A systematic review and meta-analysis. J Psychosom Res 2016; 90: 33–42. Cairns R, Hotopf M. A systematic review describing the prognosis of chronic fatigue syndrome. OccupMed(Lond) 2005; 55: 20–31. Clark L V., Pesola F, Thomas JM, Vergara-Williamson M, Beynon M, White PD. Guided graded exercise self-help plus specialist medical care versus specialist medical care alone for chronic fatigue syndrome (GETSET): A pragmatic randomised controlled trial. Lancet 2017; 6736: 1–11. Clauw DJ. Fibromyalgia A Clinical Review. 2019; 311: 1547–1555. Convertino VA, Bloomfield SA, Greenleaf JE. An overview of the issues: physiological effects of bed rest and restricted physical activity. Med &amp Sci Sport &amp Exerc 1997; 29: 187–190. Crawley EM, Gaunt DM, Garfield K, Hollingworth W, Sterne JAC, Beasant L, et al. Clinical and cost-effectiveness of the Lightning Process in addition to specialist medical care for paediatric chronic fatigue syndrome: Randomised controlled trial. Arch Dis Child 2018 Heine M, van de Port I, Rietberg MB, van Wegen EEH, Kwakkel G. Exercise therapy for fatigue in multiple sclerosis. Cochrane Database Syst Rev 2015; 2015 Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, et al. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: Prospective cohort study. Br Med J 2006 Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys A V., Taylor RR, et al. A community-based study of chronic fatigue syndrome. Arch Intern Med 1999; 159: 2129–2137. Katz BZ, Collin SM, Murphy G, Moss-Morris R, Wyller VB, Wensaas KA, et al. The international collaborative on fatigue following infection (COFFI). Fatigue Biomed Heal Behav 2018; 6: 106–121. Larun L, Brurberg KG, Odgaard-Jensen J, Price JR. Exercise	

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				therapy for chronic fatigue syndrome. Cochrane Database Syst Rev 2017; 2017: 10–13. National Institute for Health Care and Excellence. Guideline: Chronic Pain in over 16s: assessment and management. Draft for consultation [Internet]. 2020Available from: https://www.nice.org.uk/guidance/gid-ng10069/documents/draft-guideline Nijs J, Roussel N, Van Oosterwijck J, De Kooning M, Ickmans K, Struyf F, et al. Fear of movement and avoidance behaviour toward physical activity in chronic-fatigue syndrome and fibromyalgia: state of the art and implications for clinical practice. Clin Rheumatol 2013; 32: 1121–1129. Petersen MW, Schröder A, Jørgensen T, Ørnbøl E, Meinertz Dantoft T, Eliasen M, et al. Irritable bowel, chronic widespread pain, chronic fatigue and related syndromes are prevalent and highly overlapping in the general population: DanFunD. Sci Rep 2020; 10: 3273. Picariello F, Ali S, Foubister C, Chalder T. ' It feels sometimes like my house has burnt down , but I can see the sky ': A qualitative study exploring patients ' views of cognitive behavioural therapy for chronic fatigue syndrome. 2017 Ried-Larsen M, Aarts HM, Joyner MJ. Effects of strict prolonged bed rest on cardiorespiratory fitness: Systematic review and meta-analysis. J Appl Physiol 2017 Turner-Stokes L, Wade DT. Updated NICE guidance on chronic fatigue syndrome. BMJ 2020: m4774. White PD, Goldsmith K a, Johnson a L, Potts L, Walwyn R, DeCesare JC, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet 2011; 377: 823–36. World Health Organization. WHO Guidelines on physical activity, sedentary behaviour. 2020	

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Association of British Neurologists	Guideline	006	024	"Double vision and other visual disorders". The ABN considers that double vision and other focal neurological symptoms cannot be usually be explained on the basis of ME/CFS alone and require an additional explanation. We recognise that such symptoms commonly occur in ME/CFS, but it is important that clinicians are taught to look for additional explanations.	Thank you for your comment. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS. *Further investigation/differential diagnoses.* The committee agree that symptoms should be thoroughly investigated and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought.
Association of British Neurologists	Guideline	007	022	We are concerned by the recommendation to risk assess each interaction with a person with severe or very severe ME/CFS in advance to ensure its benefits will outweigh the risks to the person. We are not aware of any clinical evidence to support this recommendation. The view of the ABN is that this recommendation is neither necessary nor practical to implement. We can think of no other situation in medical practice where every interaction with a patient would be "risk assessed" in any formal way (although doctors always consider the impact of their interactions on patients as part of standard good medical practice, as defined by GMC guidance). We are concerned that the requirement to undertake a risk assessment could become a barrier to patients accessing care. We believe that standard good medical practice, and patients' existing right to decline any interaction with a health professional are sufficient to mitigate any potential risk.	Thank you for your comment. The committee agree this is good clinical practice and should happen routinely. This recommendation has been included based on Appendix 2 and the committee's experience that health and social care professionals can underestimate the impact of interactions on people with severe or very severe ME/CFS.

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Association of British Neurologists	Guideline	008 049 051	011 - 012 021 - 014 022 - 026	The recommendation that that a diagnosis of ME/CFS should be made after 6 weeks of symptoms (or 4 in children) is problematic in the light of what we know about the time course of recovery from common infections. For instance, 27 % of people with EBV infection show persistent symptoms at 3 months, but by 6 months most of these have recovered (Katz *et al.*, 2018)(Hickie *et al.*, 2006)	Thank you for your comment. *Suspecting and Diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted that the advice recommended at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted. As you note this combination of symptoms cannot be considered normal and should be investigated but the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Misdiagnosis of ME/CFS. The committee acknowledged and discussed the difficulty of removing a diagnosis of ME/CFS once it has been given. They edited the recommendations in the Diagnosis section of the guideline to ensure that the diagnosis is confirmed (and conversely, or not confirmed) by a ME/CFS specialist team. People with ME/CFS do experience delays in diagnosis and the committee

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					recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. The committee anticipate that any relevant tests would continue to exclude any other diagnoses and if symptoms resolve in the time to been seem by a ME/CFS specialist team the referral would be cancelled.
Association of British Neurologists	Guideline	008 049 052	011 - 012 018 - 021 005 - 015	There is no evidence in the review to support this recommendation that the diagnostic criteria for ME/CFS be modified to require the presence of all four core symptoms: debilitating fatigability, post-exertional symptom exacerbation, unrefreshing sleep and cognitive symptoms. In our clinical practice in neurology, we see many patients with chronic fatigue but without all of these symptoms, who have the same needs, including a NICE guideline relevant to their condition. There appears to be no evidence for a claim that patients with all four symptoms represent a discrete sub-set of those with chronic fatigue. We are particularly concerned about the emphasis on post-exertional symptom exacerbation (which the NICE reviewers stated had a sensitivity of 0.5 and specificity of 0.57). Far from being unique to ME/CFS, we often see this symptom in patients with other neurological disorders including Multiple Sclerosis. The decision to prefer the most restrictive criteria possible also appears to contradict the statement in section 2.5 of the methods "For this guideline, sensitivity was considered more important than specificity". The committee seem to go beyond their usual remit in recommending that existing diagnostic criteria for the condition under consideration should be modified. The only conceivable justification for this would be if there were strong evidence to support this, which is not the case here. The ABN would have expected the committee to work with existing diagnostic criteria.	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).

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				We recognise that these vary and describe varying and overlapping populations of patients We expected the committee to describe that heterogeneity and the evidence as it applied to different diagnostic criteria, rather than exclude a large number of patients with disabling fatigue from the guideline. The committee make a valid case for new diagnostic criteria, but it is not reasonable to then apply those criteria retrospectively to the evidence under consideration There seems to be some inconsistency between page 52 (lines 5-15) which "states that no one criteria was agreed to be better overall" and page 8 (line 11) which states that ME/CFS should be suspected when "the person has had all of the persistent symptoms" Limiting the guideline to this unvalidated subgroup does a dis-service to the many patients with severe chronic fatigue symptoms who would not meet this arbitrary definition. Importantly, this reliance on a particular set of diagnostic criteria seems to have played a central role in the approach to the evaluation of the clinical trial evidence. Trials which did not use these criteria were down-graded even though they used the standard, accepted diagnostic criteria for ME/CFS at the time of the trials. This has led to huge amount of robust clinical evidence effectively being given almost no weight by the committee, with the end result that the guidelines on treatment are primarily based on opinion rather than evidence.	*Suspecting and (mis)diagnosing ME/CFS* See Evidence review D-diagnosis for the evidence. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. We note that section 2.5 of the methods manual refers to diagnostic accuracy tests, however the in the discussion section of Evidence review D- diagnosis there is further discussion about sensitivity and specificity in the context of the development of criteria, noting that here specificity is important. This section also includes a discussion on the heterogeneity in the study populations. The committee discussed the potential harm of applying the recommendations in this to people that are misdiagnosed with ME/CFS. For example, and as noted in many stakeholder comments, for other conditions physical activity and exercise is recommended as a part of the management of symptoms such as pain. In this guideline it is clear that if people with ME/CFS have these symptoms this management approach is not appropriate. For this reason the committee agreed it was very important to ensure that only people that meet the diagnostic criteria use these guidelines. In addition misdiagnosis may result in people not receiving appropriate treatments. The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. *Evaluation of the data*

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					the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported. Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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Association of British Neurologists	Guideline	010 051	017 - 020 003 - 012	Here, and elsewhere in the guidelines, there is a bias towards the benefits of rest and potential harms of activity that we do not believe is supported by evidence. The guideline states that "the committee made a recommendation to give people advice on symptom management drawn from their own knowledge and experience". We note that, in the absence of direct clinical trial data, the usual approach should be to extrapolate from other data or consider a range of expert opinion. We believe that clinical evidence on treatment suggests that approaches based on graded activity can be more effective for some patients than approaches focusing on staying within an "energy envelope". There is a wide range of clinical expert opinion in this area. The committee do not seem to have sought this range of clinical expert opinion, but have relied primarily on their own personal views. We feel that the committee's failure to consider this indirect evidence and a range of expert opinion is manifestly unreasonable. Making a recommendation that goes against standard rehabilitation practice in other neurological disorders should require strong evidence, which was not presented here.	Thank you for your comments. The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. This has been clarified in the discussion section. *Energy envelope* After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *Advice to rest* The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in

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					the advice for people with suspected ME/CFS section of the guideline. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
Association of British Neurologists	Guideline	012 022	021 017	We agree that personalised management plans should include self-management strategies. However, listing energy management as the only example of self-management implies that this is the most effective approach. Many other self-management approaches exist. Whilst expert opinion differs on which are the most effective, there is certainly no evidence to justify this emphasis on energy management.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason. See Evidence reviews G and H for the evidence and committee discussion on self- management strategies.
Association of British Neurologists	Guideline	014	019 - 024	We are concerned that this advice to patients is incorrect and could be harmful. It is misleading to state that only "a small proportion" of people recover. It is the case that the majority of people with ME/CFS remain symptomatic but for patients who do not fully recover, treatments can result in worthwhile improvements in quality of life and social and occupational functioning, for example 39% in one systematic review of 14 studies(Cairns and Hotopf, 2005). There is also evidence that beliefs that recovery is not possible can themselves be a barrier to recovery in ME/CFS (Cairns and Hotopf, 2005). We can think of no other disease in which clinicians are advised to emphasise to patients that their condition is incurable. Even in conditions from which people *never* recover (like motor neurone disease) we would emphasise positive approaches to symptom management and improving quality of life. Clinicians should be realistic but there is a significant risk of harm with this recommendation.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet points and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Association of British Neurologists	Guideline	024 025	007 - 024 001 - 003 009 - 011	We are concerned that the guideline recommends energy management as the key management approach for ME/CFS: this is not based on evidence and is only one of a range of	Thank you for your comment.

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		 026 061	001	approaches that may be helpful for different patients. We agree that energy management may be helpful for some people with ME/CFS, but also feel that other approaches (included graded activity) can be helpful. Energy management approaches could be harmful to some patients, by becoming a barrier to recovery. We note that, in the absence of direct clinical trial data, the usual approach should be to extrapolate from other data or consider a range of expert opinion. We believe that clinical evidence on treatment suggests that approaches based on graded activity can be more effective for some patients than approaches focusing on staying within an "energy envelope". There is a wide range of clinical expert opinion in this area. The committee do not seem to have sought this range of clinical expert opinion but have relied primarily on their own personal views. Indeed, the guidelines states on page 61, line 1, that the recommendations were based on the committee's "own experience". We feel that the committee's failure to consider this indirect evidence and a range of expert opinion is manifestly unreasonable. Making a recommendation that goes against standard rehabilitation practice in all other neurological disorders should require strong evidence, which was not presented here.	This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the commissioned report on children and young people) and their own experience. The committee have recommended that a physical activity or exercise programme may be offered to people with ME/CFS who feel ready to progress their physical activity beyond their current activities or who would like to incorporate physical activity or exercise into the managing their ME/CFS. Such a programme should start by establishing a physical activity baseline at a level that does not worsen symptoms, initially reducing physical activity to be below this baseline level, which should be successfully maintained for a period of time before any attempt to increase it. Flexible adjustments should then be discussed, agreed and made to a person's physical activity. The committee recognised that although graded exercise therapy is not recommended it was important that people with ME/CFS have access to a ME/CFS specialist team to provide support with physical activity and exercise programmes where appropriate. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with

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					ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. We disagree there is a reliance on individual opinion in this guideline and this has influenced the recommendations. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence , in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership reflects the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Association of British Neurologists	Guideline	024 060	004 - 005 006 - 008	We believe it is incorrect to state that there is no current treatment for ME/CFS. There is evidence from randomised controlled trials that cognitive behavioural therapy (CBT) and graded exercise therapy (GET) can be effective for some patients, albeit with a relatively modest effect size. These trials were given little weight in the guideline for reasons that simply do not add up. The flaws in this reasoning are discussed in more detail in our comments on the specific recommendations on CBT and GET. Even it were accepted that these factors should be considered when interpreting the trial data, they are certainly not sufficient to justify giving so little weight to the evidence that the recommendations are based primarily on opinion. Whilst we appreciate that the committee must weigh different sources of evidence in reaching a conclusion, the ABN feels the way evidence was weighed in this case is manifestly unreasonable.	*Thank you for your comment.* *Cure or treatment* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				We also feel that it is unhelpful to talk about "cure". This term is rarely used in any neurological disorder. As neurologists, we would usually use terms such as 'improvement' or "recovery" which is also preferred by many patients. Many patients with ME/CFS do improve (Cairns and Hotopf, 2005)	
Association of British Neurologists	Guideline	025	004 - 022	We agree that many individuals with ME/CFS need help with managing rest and activity and are helped by learning to avoid 'boom and bust'. However, we are particularly concerned that the emphasis on rest in this recommendation may be harmful. The evidence that too much rest may be harmful in ME/CFS comes from a number of sources, in particular our knowledge of the physiological effects of rest across a whole range of conditions(World Health Organization, 2020)(Ried-Larsen *et al.*, 2017)(Convertino *et al.*, 1997). There is also evidence that fear and avoidance of physical activity can be a barrier to recovery in ME/CFS (Nijs *et al.*, 2013)(Goldsmith 2015) Throughout, the guideline emphasises the benefits of rest, and the risks of activity in a way that appears unbalanced.	Thank you for your comment. The committee agreed that rest was an important part of managing activity in people with ME/CFS. The role of rest and sleep are further addressed in section 1.12 and the rationale provides further information on this.
Association of British Neurologists	Guideline	027	021 - 023	We are concerned that there is insufficient evidence to support this recommendation and that it may be harmful. For some people with ME/CFS, especially those with milder symptoms, unstructured exercise could he a helpful part of their management. Exercise appears especially helpful in chronic primary pain (a condition with substantial overlap with ME/CFS) and which has been recommended by current draft NICE guidelines(National Institute for Health Care and Excellence, 2020). We recognise the controversy in this area, and that there is a wide range of expert opinion, but there is no rationale for the committee preferring one expert opinion over others. If there is considerable disagreement and uncertainty, it is not reasonable for NICE to make a "do not" recommendation without evidence to support it.	Thank you for your comment. After considering the stakeholder comments this has been edited to,'do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.' Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may

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					feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Pain* The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS To note the committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ‘ chronic primary pain' is a different population to that of people with ME/CFS and that the management section does

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					not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion.
Association of British Neurologists	Guideline	027 028 034 063 067	024 001 - 009 001 - 005 002 - 020 023 - 029	We are very concerned that NICE has made a "do not" recommendation for all management approaches based on physical activity, including GET. We fear that this will prevent people with ME/CFS from accessing an evidence based treatment that can improve fatigue, physical functioning and quality of life for some people with the condition (albeit with a relatively modest effect size). The recommendation gives insufficient weight to evidence from randomised clinical trials showing the effectiveness of GET in ME/CFS. The committee were aware of these trials, but have chosen to disregard them for the reasons outlined below. There is no mention of the trial data in the section on "why the committee made these recommendations" (page 63 lines 2-20) We believe that this decision was manifestly unreasonable. A key reason given for downgrading the importance of these trials was "population indirectness" (see section 1.2.5.1 of Evidence Review D). The committee decided to downgrade trials using diagnostic criteria for ME/CFS which do not include post-exertional symptom exacerbation as an essential criterion. We believe this decision simply does not add up. The committee's belief that the trial populations may not accurately represent the ME/CFS population seems to be based entirely on opinion rather than evidence. We believe this position is untenable for the following reasons: - Most patients in the trials would have met diagnostic criteria for ME/CFS that included post-exertional symptoms exacerbation. - In the PACE trial 88% of participants reported post-exertional malaise. The trial was still favourable to CBT and GET using London criteria for ME/CFS which insist	Thank you for your comment. Your assertion that the committee has made a "do not" recommendation for 'all management approaches based on physical activity' is incorrect. Recommendations 1.11.9 and 1.11.10 detail the types of physical activity and exercise programmes that should not be offered. Recommendation 1.11.11 explicitly states that a physical activity or exercise programme may be considered in certain circumstances, and Recommendation1.11.12 tells practitioners to tell people with ME/CFS that some people have found such programmes to be useful. The committee reviewed the trials exercise therapies in ME/CFS including GET where these met the agreed evidenced review protocol, and assessed their quality according to the GRADE Criteria as laid out in the current NICE methodology (See Developing NICE guidelines: the manual. Process and methods [PMG20] Published: 31 October 2014 Last updated: 15 October 2020 for further details). The committee considered a wide range of evidence, including that from published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature.

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				on post-exertional malaise(White *et al.*, 2011). In this trial post-exertional malaise fell from 84% to 63% in the adaptive pacing therapy group, from 84% to 49% in the CBT group, from 76% to 48% in the GET group. (White *et al.*, 2011) - The assertion that post-exertional symptom exacerbation is a vital part of diagnostic criteria is a contested one. There is no evidence that patients with chronic fatigue who report this symptom differ systematically from those who do not (and indeed it is not easy to define). Nor is post-exertional symptom exacerbation unique to ME/CFS. It occurs at a low level in the population and in association with fatigue in other neurological disorders including multiple sclerosis. - These trials used accepted diagnostic criteria, which remain the most widely used diagnostic criteria today (the CDC 1994 criteria and the Oxford Criteria). By definition, the trials could not have used diagnostic criteria which have been newly proposed by the committee in this guideline. - The GETSET trial, which did use diagnostic criteria that required the presence of post-exertional symptom exacerbation also showed a benefit of GET (Clark *et al.*, 2017) It is particularly unusual for a NICE guideline to choose to disregard the results of a Cochrane review. In this case, the Cochrane review of exercise interventions(Larun *et al.*, 2017) was excluded on the basis that is "did not include all critical outcomes specified in this review protocol and included study populations where not all participants had ME/CFS." It is unclear which critical outcome was not included (we wonder if it could be mortality) but it seems inexplicable that this would lead to the entire review being excluded. It is simply incorrect to say that "not all participants had ME/CFS". Participants did have ME/CFS	See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. The decision to include post exertional malaise (sometimes referred to as post exertional symptom exacerbation) as an essential part of the diagnostic criteria is entirely consistent with recent publications. Post Exertional Malaise/PESE is a required component of the Revised Canadian consensus criteria (Jason

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				according to accepted criteria, just not necessarily according the novel criteria preferred by this committee. In addition, we note that the committee used the latest available data point from trials rather than the pre-specified endpoint. The ABN does not consider this approach to be scientific or reasonable. After the end of trials many patients in the control group choose to have additional treatment, reducing the power to detect a treatment effect at later time points. Whilst it is reasonable to consider the latest available data, it is unreasonable to give this greater weight than data at the pre-specified ending of the trial. We also believe that, having down-graded the clinical trial evidence, the committee unreasonably chose to favour one particular set of patient and expert opinion without making reasonable efforts to seek a range of expert opinion and patient testimony. For instance, were the opinions and experiences of patients who had participated in these trials, or the experiences of patients who had improved sought? The potential harms of graded exercise in ME/CFS have been emphasised throughout this guideline, but this emphasis appears to be based on the opinion of the committee rather than on evidence. The press release from NICE about the guideline states "Because of the harms reported by people with ME/CFS, as well as the committee's own experience of the effects when people exceed their energy limits, the draft guideline says that any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy (GET) should not be offered for the treatment of ME/CFS". The guideline itself states at page 63 lines 6-7 that this judgement was based on the "committee's own experience". This demonstrates that the committee's own beliefs about the harms of GET were a key driver of the guideline's recommendations.	2010), the International consensus criteria (Carruthers 2011), and the IOM diagnostic criteria (Clayton 2015). To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. The committee's understanding that the populations in some trials may not accurately represent the ME/CFS population is based entirely on the written evidence in the publications that they reviewed. The assertion from the consultee that 'Most patients in the trials would have met diagnostic criteria for ME/CFS that included post-exertional symptoms exacerbation'. is conjecture. The London Criteria as used in the PACE trial ('PACE trial protocol: Final version 5.0, 01.02.2006 p188) does not include post exertional malaise. On the basis of the written criteria used to assess participants in the PACE trial the committee could not establish that participants experienced post exertional malaise. The assertion that the Oxford Criteria, used in the PACE trial, remains the most widely used diagnostic criteria today is questionable, especially given the comment from the National Institutes of Health (Green 2014) that continuing to use the Oxford definition 'may impair progress and cause harm' and the recommendation 'that the Oxford definition be retired' (Green 2014) .

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				We believe this emphasis on the potential harms of graded exercise is unreasonable. There is strong evidence from clinical trials that GET is not harmful: drop-out rates from therapy in these trials were very low and deterioration in symptoms was not more common in GET group than in controls (White *et al.*, 2011; Clark *et al.*, 2017). For example, in the GETSET trial 6% of both intervention and control groups reported being 'much or very much worse'. We recognise that GET is not appropriate for everyone with ME/CFS, and that some people have had negative experiences of this approach (especially if it is not delivered well). However, it is crucial that this observation does not allow us to lose sight of a larger group of patients for whom it can be effective. By definition, GET is a collaborative approach that can only work if patients choose to participate. We certainly would not advocate that anyone who did want to undertake GET should be pressurised to accept this form of treatment (consistent with good medical practice in any condition). However, we know from clinical trial data and our clinical experience in neurology that there is a large group of patients who want to access this treatment. This recommendation is a marked change from the previous NICE guideline on CFS/ME, which recommended GET. There was substantial scrutiny of this guideline: a judicial review to challenge it was not upheld. The rationale for this dramatic change in a recommendation which is based on essentially the same evidence base is insufficient and fundamentally flawed. NICE processes require that committees should seek to ensure, as far as possible, that their judgements are applied consistently. In this case, the guidelines concerned the same group of patients and considered substantively the same evidence base. There would therefore have to be a strong justification for any	The GETSET trial (Clark 2017) was not downgraded for indirectness. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population > 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken and the analysis. There was no substantive impact on the results and interpretation of the evidence. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. The comment about the inclusion criteria for the review is correct. The review included studies where more than 90% of the participants had a primary diagnosis of CFS according to the criteria that participants had 'medically unexplained', disabling, distressing and prominent fatigue for more than 6 months. Five of the studies eight studies included in the review used the Oxford diagnostic criteria, and therefore may have included patients who did not have PEM. You comment that the current draft guideline is 'based on essentially the same evidence' as the previous NICE guidance (CG53) published in 2007. A review of the Effectiveness Evidence Tables (Appendix D) shows that the majority of

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				inconsistency. In fact, the justification given seems completely flawed. Implementation of these guidelines would prevent people with ME/CBT from accessing an intervention that can be effective for some people.	included studies were published after 2007 (41/75). The current guideline also included further evidence in the form of published peer review quantitative and qualitative papers, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports. The assertion that the guideline concerns 'the same group of patients and considered substantively the same evidence base' as CG53 is-incorrect. In addition this guideline has updated the 2007 guideline using Developing NICE guidelines: the manual Process and methods [PMG20] Published: 31 October 2014 Last updated: 15 October 2020.
Association of British Neurologists	Guideline	028 029	023 - 029 001 - 005	We are concerned that the recommended approach to physical activity is biased towards "staying within an energy envelope" rather than graded activity (even though clinical trial evidence is more supportive of the latter, and there is a wide range of expert opinion on this question.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical

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					effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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Association of British Neurologists	Guideline	028	012 -015	We are concerned that this recommendation is essentially discouraging physical activity programmes. It is obviously true that a physical activity programme could only ever be used if a patient wanted to take part in this. This does not need to be stated.	Thank you for your comment. The committee disagree that this recommendation is essentially discouraging physical activity programmes, it sets out when a physical activity or exercise programme should be delivered.
Association of British Neurologists	Guideline	028	019 - 022	Good medical practice always requires the risks and benefits of an intervention to be explained to patients. However, we are concerned that this recommendation implies that there is clinical equipoise about whether physical activity is beneficial or harmful. This is incorrect. We know that encouraging activity is central to rehabilitation in all neurological disorders as well as other physical conditions. There is no biologically plausible reason that these same mechanisms would not also apply in CFS/ME. We would therefore need robust evidence of harm from exercise in ME/CFS to justify any recommendation that goes against established rehabilitation practice. Such evidence has not been presented. Exercise appears especially helpful in chronic primary pain (a condition with substantial overlap with ME/CFS) and which has been recommended by current draft NICE guidelines(National Institute for Health Care and Excellence, 2020). There is also evidence that fear and avoidance of physical activity can be a barrier to recovery in ME/CFS(Nijs *et al.*, 2013) (Nijs 2013, Goldsmith 2015)	Thank you for your comment. Physical activity and ME/CFS It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.

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					Chronic pain The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion.
Association of British Neurologists	Guideline	028	010 - 011	Whilst there is limited evidence for these approaches, we do not believe there is sufficient evidence to justify a "do not" recommendation. In particular, the one randomised trial of the lightning process does support its effectiveness(Crawley *et al.*, 2018). Even if the committee judged that this evidence was weak, it is difficult to see how it could be reasonable for a committee to go from this evidence base to a "do not" recommendation	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)
Association of British Neurologists	Guideline	029 030	017 - 022 001 - 002	We are concerned that the recommendations on rest are unbalanced, and make no mention of the physiological harms of rest(World Health Organization, 2020)(Ried-Larsen *et al.*, 2017)(Convertino *et al.*, 1997) We recognise that the relative benefits and harms of rest in ME/CSF are controversial, but can see no reasonable justification for the committee's decision to favour specific expert opinion over other expert opinion and evidence on this question.	Thank you for your comment. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep, this would include the risks and benefits, and personalised sleep management advice.
Association of British Neurologists	Guideline	030	015	We believe that is not appropriate for the guideline to refer to the NICE guideline on neuropathic pain, as there is no evidence of nerve or brain damage in the pathophysiology of ME/CFS (and pain in ME/CFS is not necessarily neuropathic in character). We believe that reference to the NICE guideline on chronic primary pain would be more appropriate. There is strong evidence for	Thank you for your comment. *Neuropathic pain* The committee disagree, people with ME/CFS report many different types of pain, neuropathic pain is one of them. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience.

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				overlap between ME/CFS and chronic primary pain which includes fibromyalgia (Jason *et al.*, 1999).	*Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any symptoms or co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Association of British Neurologists	Guideline	034 067	001 - 005 023 - 029	We are very concerned that the guideline states that CBT should not be offered as a treatment for ME/CFS. We fear that this will prevent people with ME/CFS from accessing an evidence based treatment that can improve fatigue, physical functioning and quality of life for some people with the condition (albeit with a relatively modest effect size). The recommendation gives insufficient weight to evidence from randomised clinical trials showing the effectiveness of CBT to treat fatigue and physical function in ME/CFS. The committee were aware of these trials, but have chosen to disregard them (there is no mention of the trial data in the section on "why the committee made these recommendations") We believe that the justification for the down-grading of these trials is flawed. A key reason given for downgrading the importance of these trials was "population indirectness" (see section 1.2.5.1 of Evidence Review D). The committee decided to downgrade trials using diagnostic criteria for ME/CFS which do not include post-exertional symptom exacerbation as an essential criterion. We believe this decision simply does not add up. The	Thank you for your comments. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is offered to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS and to reduce the psychological distress associated with having a chronic illness. *Indirectness*

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				committee's belief that the trial populations may not accurately represent the ME/CFS population seems to be based entirely on opinion rather than evidence. We believe this position is untenable for the following reasons: - Most patients in the trials would have met diagnostic criteria for ME/CFS that included post-exertional symptoms exacerbation. - In the PACE trial 88% of participants reported post-exertional malaise. The trial was still favourable to CBT and GET using London criteria for ME/CFS which insist on post-exertional malaise(White *et al*., 2011). In this trial post-exertional malaise fell from 84% to 63% in the adaptive pacing therapy group, from 84% to 49% in the CBT group, from 76% to 48% in the GET group. (White *et al*., 2011) - The assertion that post-exertional symptom exacerbation is a vital part of diagnostic criteria is a contested one. There is no evidence that patients with chronic fatigue who report this symptom differ systematically from those who do not (and indeed it is not easy to define). Nor is post-exertional symptom exacerbation unique to ME/CFS. It occurs at a low level in the population and in association with fatigue in other neurological disorders including multiple sclerosis. - These trials used accepted diagnostic criteria, which remain the most widely used diagnostic criteria today (the CDC 1994 criteria and the Oxford Criteria). By definition, the trials could not have used diagnostic criteria which have been newly proposed by the committee in this guideline. In addition, we note that the committee used the latest available data point from trials rather than the pre-specified endpoint. The ABN does not consider this approach to be scientific or reasonable (see below). After the end of trials many patients in	See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. After considering the stakeholder comments the committee agreed to revisit the quantitative and qualitative evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population > 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *London criteria* The London Criteria as used in the PACE trial ('PACE trial protocol: Final version 5.0, 01.02.2006 p188) does not include post exertional malaise. On the basis of the written criteria used to assess participants in the PACE trial the committee could not establish that participants experienced post exertional malaise.

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				the control group choose to have additional treatment, reducing the power to detect a treatment effect at later time points. Whilst it is reasonable to consider the latest available data, it is unreasonable to give this greater weight than data at the pre-specified ending of the trial. It is important to emphasise that these trials were not using CBT as a treatment for psychological distress, but as a treatment for the disorder itself. Typically, the primary endpoints were fatigue ratings scales and measures of physical functioning. Whilst CBT may also have benefits for well-being and non-specific benefits in supporting people to cope with chronic illness, it is misleading to imply that this was the primary purpose of CBT in these trials. We also believe that, having down-graded the clinical trial evidence, the committee unreasonably chose to favour one particular set of patient and expert opinion without making reasonable efforts to seek a range of expert opinion and patient testimony. At page 67, lines 24-25 they say only that the recommendation was based on "criticisms in the qualitative evidence". Were the opinions and experiences of patients who had participated in CBT trials sought? There is qualitative evidence of positive patient experiences of CBT(Picariello *et al.*, 2017) Implementation of these guidelines would prevent people with ME/CBT from accessing an intervention that can be effective for some people.	
Association of British Neurologists	Guideline	034	012	We believe the use of the word "curative" is unhelpful here. This term is rarely used in any neurological disorder. As neurologists, we would usually use the terms 'improvement' or "recovery" which is also preferred by many patients. We would suggest changing this bullet point to "CBT can help some people to recover".	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
Association of British Neurologists	Guideline	034	013	It is misleading to state that CBT in ME/CFS is "designed to improve well-being". CBT for ME/CFS is primarily designed to treat the core symptom of the disorder, fatigue, and its effect on daily living. Trial evidence suggests that it improves fatigue and physical functioning as well as quality of life(White *et al.*, 2011) We are concerned that this statement implies that CBT would only help people who are experiencing significant psychological distress from their CBT/ME. This is an incorrect interpretation of the evidence.	Thank you for your comment. After considering the stakeholder comments, this has been deleted and the next bullet point edited to,' aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness'.
Association of British Neurologists	Guideline	035	019 - 021	The principles of consent mean that all treatments are only given once patients are fully informed about the potential risks and benefits. We feel that the inclusion of this statement implies that CBT is a particularly risky or unproven therapy, which is incorrect.	Thank you for your comment. It is good practice to discuss the risks and benefits of any intervention and CBT is no exception. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the

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					guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Association of British Neurologists	Guideline	038	001 - 005	This guidance on managing a relapse places emphasis on increased rest and a reduced "energy envelope". Other strategies are not mentioned. The rationale for this emphasis is not clear, in a situation where it is recognised that there is a wide range of expert opinion.	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available.
Association of British Neurologists	Guideline	040	016 - 023	We support the recommendation that training programmes should represent the experiences of people with ME/CFS. We would note that it is important that this should represent the wide range of experience of people with the condition.	Thank you for your comment.
Association of British Neurologists	Guideline Evidence review	049 ref	011 - 014 ref	The statement in the guideline that "Based on both the evidence and their experience, the committee agreed that the Institute of Medicine's 2015 criteria had the best balance of inclusion and exclusion of all the 13reviewed criteria" is not consistent with the evidence review. The evidence review found no evidence to support a preference for any particular set of diagnostic criteria. It seems that this statement is, in fact, wholly based on the opinion of the committee. This approach might arguably be reasonable if it were simply offering advice to clinicians on diagnosis. However, in this case, the reliance on a particular set of diagnostic criteria had a major effect on the evaluation of (and weight given to) clinical trial data. This fundamentally affected	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with

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				the recommendations on treatment. Given that the evidence about the best diagnostic criteria was so uncertain that the recommendation was based on committee opinion, it is perverse that clinical trials should be given less weight based on alternative criteria having been used.	clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would be no need for the committee to address this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS.

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					The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion. The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce the number of misdiagnoses through allowing short-lived fatigue to be excluded. The committee emphasised the importance of identifying and excluding other conditions, and that these should be appropriately investigated in people with suspected ME/CFS. *PEM, indirectness and relevance* PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative

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					and qualitative evidence and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population > 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Association of British Neurologists	Guideline	050	016 - 025	We are concerned that this section does not accurately reflect how these recommendations might affect practice. Recommending the most restrictive possible diagnostic criteria (requiring the presence of all four core clinical features) is likely to make it more difficult for those who do not conform to these criteria to access treatment. In our clinical practice in neurology, we see many patients with chronic fatigue but without all of these symptoms, who still need help and support.	Thank you for your comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. There are already patients who have some of these symptoms but do not fit established criteria for an ME/CFS or an alternative diagnosis. The NHS has a duty of care for these patients even in the absence of a diagnosis. It is implicit that these patients will still need to be cared for by the NHS and might need further investigations. However, these patients are outside the scope of this guideline.
Association of British Neurologists	Guideline	050	009 - 012	We agree that ME/CFS can be difficult to distinguish from other conditions. We believe that the guideline does not place sufficient emphasis on psychiatric differential diagnoses (such as depression). This omission positively fuels stigma against people with mental health conditions.	Thank you for your comment. The committee have revised the list of differential diagnosis and added, mental health conditions: anxiety, depression or mood disorders.
Association of British Neurologists	Guideline	052 053	029 - 031 001 - 003	We are concerned that this section does not accurately reflect how these recommendations might affect practice. Shortening the required duration of symptoms to make a diagnosis will increase referrals of patients who would have recovered spontaneously from a precipitating event. For instance, 27 % of people with EBV infection show persistent symptoms at 3 months, but by 6 months most of these have recovered (Katz *et al.*, 2018)(Hickie *et al.*, 2006)	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. The committee have also added more recommendations about testing to exclude alternative diagnosis. Furthermore, the diagnostic criteria are slightly stricter than in the previous guideline. Therefore, there need not be a large increase in referrals and if patients' symptoms resolve spontaneously then appointments with the specialist ME/CFS service can be cancelled.

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					See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.
Association of British Neurologists	Guideline	060	022 -026	We believe this is an inaccurate description of the impact of these recommendations on services. In fact, the recommendations are likely to remove access to an intervention that is currently available in many specialist services, which we know can be effective for some patients. We are also concerned that the recommendation is inconsistent with the NICE guideline for chronic primary pain (currently under consultation) which recommends exercise therapy for fibromyalgia (an illness with considerable overlap with ME/CFS). This inconsistency will make the recommendation difficult to implement in clinical practice.	Thank you for your comment. After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H)

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					Throughout the guideline a holistic personalised approach to the assessment and the management of ME/CFS is and as part of this the management of symptoms should be fully explored with the person with ME/CFS. The recommendation of exercise in other guidelines, including those on primary chronic pain, highlight the need for a specialist ME/CFS team to develop a care plan for people with ME/CFS, whose treatment response is so different.
Association of British Neurologists	Guideline	060	012 - 014	We do not agree with the statement that concerns over the validity of outcome measures have made it difficult to combine results or limited the ability to draw conclusions from trial data. Cochrane meta-analyses have successfully combined data from clinical trials in ME/CFS.	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The protocols detailed what the outcomes were and the committee advised on where they could be combined.
Association of British Neurologists	Guideline	065	011	The committee seem unaware of the substantial diagnostic overlap between ME/CFS and Fibromyalgia(Clauw, 2019)(Petersen *et al.*, 2020). Fibromyalgia is defined by chronic widespread pain, which is present, as this report notes in up to 80% of individuals with ME/CFS. The other core components are unrefreshing sleep, cognitive difficulties and fatigue which are also core features of ME/CFS. It would have been appropriate for the committee to acknowledge this overlap and signpost readers to draft NICE guidelines related to chronic primary pain (fibromyalgia) which take a substantially different view of the evidence.	Thank you for your comment. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated.
Association of British Neurologists	Guideline	068	021 - 023	We believe this is an inaccurate description of the impact of these recommendations on services. In fact, the recommendations are likely to make it harder for patients with ME/CFS to access CBT, particularly if their priority is to improve their fatigue or physical functioning rather than psychological	Thank you for your comment. The committee have revised the wording of their recommendations so that they are less negative regarding CBT. However, they continue emphasise the need for patients and clinicians to be informed about the limitations of this therapy for

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				distress. We are also concerned that the recommendation is inconsistent with the NICE guideline for chronic primary pain (currently under consultation) which recommends CBT for fibromyalgia (an illness with considerable overlap with ME/CFS). This inconsistency will make the recommendation difficult to implement in clinical practice.	people with ME/CFS. We anticipate there might be a reduced demand for CBT, but it remains an important part of management that some people with ME/CFS will benefit from. That recommendations might differ to those in other guidelines, including those on primary chronic pain, highlight the need for a specialist ME/CFS team to develop a care plan for people with ME/CFS, whose treatment response is so different.
BACME – British Association for CFS/ME professionals	Appendix 3 – Expert Testimonies	013	Table: Jonathan Edwards	On page 13 at the end of the 'Implications for Recommendations' section, the conclusion of Professor Edward's Testimony is: "The only legitimate position I see is to make no recommendations for specific therapies and focus on supportive care." If this principle is to be followed, then it should apply to guidance from NICE about what should not be provided as well as what should be provided. If there is no reliable evidence to recommend CBT or GET to treat ME/CFS then equally there is no reliable evidence to advice against them either. BACME would agree that CBT and GET should not be used on the premise of treating 'faulty cognitions' or deconditioning as has been written about in many studies. However, it is entirely possible for a treatment to show benefit, or harm, that is mediated through a different mechanism than the one we expected. BACME would welcome acknowledgement from the NICE committee that clinicians who work in specialist CFS/ME services need to have particular skills to be able to operate safely in a field which does not yet have a robust evidence base. Working in this way can be made safer through better professional networking to share ideas and concerns as well as training events that allow time for discussion and sharing of knowledge. Question 3 re existing resources: BACME is working hard to provide this for the UK professional ME/CFS community.	Thank you for your comment. *Professor Edwards* Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion. *Specialist services skills* The committee agree that people with ME/CFS should have access to health and social care professionals with specific expertise and this is outlined and recommended in the multidisciplinary care section of the guideline. In addition, the committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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BACME – British Association for CFS/ME professionals	Appendix 3 – Expert Testimonies	020	Table: Mujtaba Husain	We are unclear as to why this expert testimonial has been included and how this may have influenced aspects of the guideline. The purpose of the testimony was to explore: 'The different models of multidisciplinary care, including team composition, for people with ME/CFS.' This testimony only presents one model of care which we do not feel is representative of other CFS/ME services in the UK. BACME conducted a National Services survey in 2018 which included questions regarding service structure and multidisciplinary team composition. Despite BACME submitting this document as part of the evidence review it appears to have been discounted despite it being very relevant to this issue identified as important by the NICE committee. We would urge the committee to access this survey document either from the original evidence submission or from the BACME website: BACME CFS/ME National Services Survey. This testimony gives the impression that NHS specialist CFS/ME services are operated through mental health trusts with a psychiatry led team. The BACME services survey demonstrates that out of the 42 services who completed the survey there were only 4 Psychiatrists or Liaison Psychiatrists involved in the delivery of CFS/ME care. There is a much larger number of medical professionals from non-mental health backgrounds represented in NHS CFS/ME services. BACME are concerned that this testimony also gives the impression that ME/CFS should be approached through a persistent physical symptoms service as provision of this type of service varies greatly across the country and will not always involve the comprehensive diagnostic and investigative processes referred to in this testimony. The current provision of specialist CFS/ME care within the NHS is extremely variable in terms of size of service, geographical coverage and the professional backgrounds of staff involved in running the services. This heterogenicity leads to difficulties for	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed by the committee taking into account a range of evidence. Stakeholders during the scoping process and the committee in early meetings identified areas of the scope where there was a lack of evidence. Where this is the case additional evidence can be sought to support the committee in their decision making. There are several approaches that can be taken to provide the committee with additional evidence and these include calls for evidence, expert testimonies, and in exceptional situations commissioned reports. See Developing NICE guidelines: the manual for further information on the process for including additional evidence (section 3.5 for expert witnesses). This guideline included 3 expert testimonies. Dr Husain was invited to discuss his experience of the different models of multidisciplinary care, including team composition, for people with ME/CFS. The summary of his presentation and the following committee discussion is in Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee members have their own clinical and personal experience of specialist services and the summary of their discussion acknowledges and details the different structures and MDT approaches across the NHS, this has been added to taking into account stakeholder comments and much of your comments are reflected in their discussion. *Structure of a ME/CFS specialist service* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the

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				commissioners as the cost of care can also vary greatly dependant on the structure of the team delivering the service. Without any guidance on what the structure of a specialist CFS/ME service should look like and what population size and geographical area is appropriate for a service to cover, this inequality in access to specialist care will remain within the NHS. We therefore ask the committee to acknowledge this inequity, ensure there is an expectation on commissioners to fund specialist care for people with ME/CFS within the currently existing services, and to make recommendations to explore this issue further so greater clarity can be achieved.	evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee agree there is inequity in access to ME/CFS services and throughout the guideline have made recommendations to improve access to care however it was not within the committee's remit to make specific recommendations on service design and delivery.
BACME – British Association for CFS/ME professionals	Declarations of Interest	General	General	As part of this submission we would like to draw the committees attention to an important error in the Declaration of Interest document regarding one of the NICE committee members. Michael Beadsworth is listed as being an Executive committee member of BACME with no 'interest ceased' date stated. The current BACME board has been in place since February 2019 and Mike Beadsworth has not been involved with the BACME board during that time and he does not hold current membership of our organisation. BACME would like to make it clear that no members of the current BACME board have had any involvement in the draft NICE guideline on ME/CFS and Mike Beadsworth has had no involvement in this comment submission from BACME. We would be grateful if your records could be amended to ensure this situation is clarified.	Thank you for your comment. The Declaration of Interest register has been amended.
BACME – British Association for	Equality Impact Assessment	General	General	BACME would like to bring to the attention of this NICE Guideline Development Group that there are a number of challenges affecting specific groups which make it more difficult and, in many cases, not possible for preliminary recommendations to be	Thank you for your comment. *Access to services*

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CFS/ME professionals				in place. The preliminary recommendation that severely affected patients receive home visits is not possible for services to implement due to limited resource. The geographical spread of services across the UK is a significant factor affecting access to care, please see the BACME National Services Survey. While this draft guideline includes some special considerations where children and young people are concerned, overall, this draft guideline is considered inappropriate for use with children and young people due to its focus on severely affected adults and its message of no hope and no cure.	The committee agreed that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care particularly for the conformation of diagnosis and the development of the care and support plan. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms and that some people with severe ME/CFS may not choose home visits finding other method of consultation better for them. The committee agree that there is variation in the delivery of home visits across the NHS but these recommendations will provide equity of access for this group, particularly for people with ME/CFS who are housebound. *Children and Young people* With every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to develop recommendations that were individualised but reflected the variation in the impact and severity of symptoms that people with ME/CFS experience. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative

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					tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.) *Cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
BACME – British Association for CFS/ME professionals	Evidence Review G	210	Table 68	The Forward ME survey 2019 has a high level of risk of research bias and yet has no concerns listed regarding bias. We think that this should be amended, based on the evidence presented below. BACME contacted NICE at the time that this study was being conducted as it was marketed as having been commissioned by NICE. We were concerned that the tone and language used was biased and ran the risk of undermining trust in NHS services. We could also see there was a significant risk of selection bias regarding the people completing the survey and how it was unlikely to capture the voice of patients who have had beneficial treatment delivered by an NHS service.	Thank you for your comment. We agree there are important limitations that have been considered. The Forward ME survey 2019 has been downgraded for concerns methodological limitations due to concerns over the recruitment strategy uses, the data collection method (including open ended questions focusing on negative aspects of treatment) and concerns over data analysis as specified in the qualitative evidence table for the survey in Appendix D on Evidence review H. This has been accounted in the assessment of confidence of review findings that the survey contributes to. The limitations in the evidence have been brought to the committee's attention and taken into account in decision making. In addition to this, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to and in

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				The Survey only invited open ended qualitative comments about GET which were negative experiences. There was not an option in this survey to offer comments about positive experiences. This significant bias is not reported in the summary on page 21. We think that this issue should be clearly documented in the Guideline, so that people reading the Guideline in the future are aware of this limitation. It should also be noted that this survey had small numbers of patients compared to the actual number of patients who are seen in NHS specialist services every year. For example, there are 50 survey respondents from Bristol and 47 from Gloucestershire, during a period (2007-2019) when the NHS Service covering Bristol and Gloucestershire assessed approximately 6,000 patients. The survey therefore represents only 1.6% of NHS patients seen in the services covering this area. The fact that this survey does not represent the experiences of approximately 98% of NHS patients should be clearly stated. There is also no comment about the potential for bias in recruitment method (which included social media: see Bristol CFS/ME Service reference 58 for an indication of the impact of this type of recruitment). We think that there should be a clear comment to state that the survey cannot be seen to represent the experiences of the majority of patients attending NHS Services. Finally, the Survey asked whether GET improved symptoms, therefore evaluating GET as if it was a symptom-relieving treatment like Amitriptyline, and not a rehabilitation approach aiming at improving function. Does the committee think that these shortcomings might influence any other sections of the Guideline?	turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See evidence review H Appendix on PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed that in order for this criterion to be adequately met, self-reporting of PEM would not be sufficient and 95% of participants need to have been diagnosed by a health professional as having PEM. The Forward ME 2019 survey did not meet this criterion as 98.5% self-reported their experience of PEM. As a result, evidence from the survey was further downgraded for concerns over the applicability of the population, which is reflected in the relevance rating component of the assessment of confidence in the findings. This resulted in further downgrading the confidence in the relevant review finding from Moderate to Low quality. The committee agreed methodological shortcomings are important and this approach has been followed throughout the guideline to ensure such shortcomings have been accounted in the assessment of confidence in the evidence/ evidence quality which contributes to decision making along with the variety of factors including the different types of evidence, the balance between benefits and harms, economic considerations, equality considerations and the committee's clinical expertise (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
BACME – British	Evidence Review G	215	Table 72	Two themes have been conflated here. The "Too difficult" theme includes a) Most found following the programme to be "hard	Thank you for your suggestion. Based on the wealth and variability of the information available, similar findings from

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Association for CFS/ME professionals				work". We suggest that this is renamed to be the "Hard work" theme. It also includes b) a reiteration of the issues related to baselines not being collaboratively established by the patient and therapist. This is not a problem which is inherent to the rehabilitation, it is an indication of a lack of collaboration to establish sustainable baselines.	different studies have been synthesised into different themes to reflect similar experiences emerging across studies. The evidence suggests that the fact that the level of exercise was selected by the therapist also made the intervention difficult, so this element has been interpreted to contribute to the difficulty theme as it led to the intervention being perceived as 'hard to follow' (Cheshire 2020). However, the lack of sufficiently deep information there is to support this theme, as well as the possibility that 'hard work' may not necessarily reflect the same experience of difficulty emerging across studies, have been taken into account in the assessment of confidence in the theme as is reflected in the description of the themes' assessment of confidence both in the evidence review's narrative summary of the review findings and in the qualitative evidence summary footnotes
BACME – British Association for CFS/ME professionals	Evidence Review G	268	Table 85	Regarding baseline activity levels and false starts. There is an item which is probably drawn from Gladwell 2013 (referenced in the Guideline as Gladwell 2014, perhaps in error) stating "but baseline levels were not experienced as sustainable". Unfortunately, this oversimplifies the detail in the original paper, where baseline setting was considered by some to be a positive, and by others a negative aspect of rehabilitation. The section in the original paper about unsustainable baselines as a negative aspect of rehab is followed by this sentence: "A recurring theme across reports was the level of exercise being selected by the therapist, and experienced by patients as too difficult." The issue here is that these were not actually baselines, because a baseline should be agreed between the patient and the therapist and should by definition be sustainable. The problem was that the therapists thought that they could set baselines for the patient, not that baselines per se are unsustainable. This is an example of poor quality rehabilitation in some settings, not a problem with baselines as such. We suggest that this section is amended to reflect the complexity of this issue.	Thank you for your comment. Based on the wealth and variability of the information available, a number of different themes usually emerge from the same study, often reflecting different experiences that can be positive and negative. We have thoroughly been through the information reported in all papers to extract all that reflect people's experience of the interventions they received and organise them into different themes to bring to the committee's attention. The committee acknowledges that experiences vary between different people. However, some people did experience difficulty with baselines with some explicitly reporting experiencing a pressure to comply with activity levels that were not sustainable, and exercise was experienced as too difficult when selected by the therapist. This experience has been synthesised together with findings from the Cheshire study illustrating a similar experience of difficulty following the exercise program under the theme regarding baseline activity levels and false starts. However, this does not mean that positive experiences also reported in the Gladwell paper have been discarded. In particular, confidence in the 'baseline activity levels and false starts' theme has been downgraded for concerns about

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					coherence to account for the emerging positive experiences of some people and in particular descriptions related to ease and benefits of setting baselines that differ from reported experiences of unsustainability and 'false starts'. Apart from accounting for positive experiences in the assessment of confidence of the aforementioned theme, reported experiences of finding rehabilitation helpful for example in setting realistic and manageable targets have also been extracted from the Gladwell study (see Qualitative evidence tables in Appendix D, Evidence review H) and these have been summarised under themes such as 'support for self-management' and 'routines and goals' that reflect peoples' positive experiences. All findings reflecting both positive and negative experiences have been considered by the committee who acknowledge the complexity of this issue in the recommendations.
BACME – British Association for CFS/ME professionals	Evidence Review G	323	005	We would suggest that there are two issues arising from to this paragraph: "The committee discussed that pacing is the main self-management tool used by many people with ME/CFS and noted pacing is often used as one of the first steps of interventions such as cognitive behavioural therapy (CBT) to stabilise a person's activity levels. The committee considered the evidence regarding the best self-management strategy is unclear and that in their experience people with ME/CFS use their own individual self-management strategies without the need for a specific intervention. Taking this into account the committee did not make a recommendation for any particular self-management strategy. The committee agreed it is important that people with ME/CFS are offered information about self-management strategies and the qualitative evidence showed that people valued this type of information and support. The committee noted that energy management includes some of the components that are identified in this type of intervention (such as activity monitoring)	Thank you for your comment. Although the quantitative evidence identified was limited and no evidence was identified on people's experiences of self-management interventions in the qualitative review of experiences of interventions, evidence identified for other interventions that encouraged self-management techniques showed that people with ME/CFS appeared to value and benefit from this type of support. After considering the evidence identified for self-management, as well as the lack of information and support people with ME/CFS report in managing their symptoms emerging from Evidence review A and their clinical experience, the committee agreed the evidence was unclear but recognised the benefits of self-management strategies for people with ME/CFS and the importance of having access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (see Evidence review G for the committee discussion on self-management strategies) The committee recognise people may benefit from different self-management strategies and that these should be discussed and

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				and reflected these components in the recommendations on energy management and flares and relapse." Firstly, we suggest that it would be helpful to expand the focus of self-management to the 75 self-management skills which have been identified through research into long-term condition management (Schulman-Green et al, 2012). Pacing is only one of those 75 skills, together with activity management, and setback management but there are many other self-management skills which could be considered in relation to ME/CFS, which may be found to be beneficial. We suggest that this wider set of self-management skills be considered in future research, with a suggestion that a self-management intervention could be co-constructed for evaluation. We also suggest that the outcomes of this self-management intervention should include self-efficacy and a measure of sustainable function, including frequency/severity of flares (or dips) and relapses rather than a primary focus on function, or symptoms, as self-management as a complex intervention with a set of complex outcomes, which are context-dependent. Secondly, we suggest that it should be noted that the committee's experience that "people with ME/CFS use their own individual self-management strategies without the need for a specific intervention" does not reflect the experience of recently diagnosed patients attending NHS Services. Reference: Schulman-Green, D., S. Jaser, F. Martin, A. Alonzo, M. Grey, R. McCorkle, N. S. Redeker, N. Reynolds and R. Whittemore (2012). "Processes of Self-Management in Chronic Illness." Journal of Nursing Scholarship 44(2): 136-144.	agreed with the person with ME/CFS to support them in developing a care and support plan that is tailored to their individual needs as reflected in the recommendations.
BACME – British Association for	Evidence Review H	General	General	Excluded Studies We are concerned that many key studies have been downgraded and excluded for not having relevant themes. There	Thank you for your comment. All references identified through systematic searches of the literature were assessed for inclusion

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CFS/ME professionals				are inconsistencies in the criteria applied. The National Outcome Database many specialist services have populated over several years reflects the outcomes and narrative of a significant number of patients who have experienced holistic and individualised therapeutic interventions with noticeable improvements recorded. However, all references have been discounted. Conversely, the voices of a carefully selected minority through the committee is worryingly regarded as definitive experience. In particular quantitative studies where patients have done well or relatively well have been omitted. Members are concerned that evidence supporting existing and successful specialist practices that patients report have positively impacted their condition are universally omitted. In our combined extensive clinical experience patients seen in our service have done well in terms of measurable, improved outcomes and data exists to support these claims. Question 1 re challenging to implement by specialist services: Members are left wondering what they can base credible and safe specialist practice upon given that therapeutic approaches research with positive outcomes are not regarded as valid to investigate and reference. Question 3 re existing resources: BACME are the ideal body to work with to synthesise data on the delivery of UK based specialist practice for patients with ME/CFS to ensure the final guideline does include reliable treatment options appropriate for Primary Care to employ and to promote new specialists to the field to practice safely. We find it concerning that the committee placed so much importance on a systematic review that contained 15 relevant studies all of them qualitative. The majority have small samples, lack scientific rigour, reliability and generalisability. A limited number of service users does not fully reflect the heterogeneity	in the evidence reviews, based on the inclusion/exclusion criteria of the protocols that had been developed in advance for each review question. Qualitative evidence meeting the review protocol criteria (in terms of the study design used, the population included, the intervention examined) but from which there was no relevant information to extract to illustrate the review topic, were excluded as there was no information that would contribute to illustrating the phenomenon of interest and answering the review question. Where evidence has been downgraded for concerns over relevance, there are different reasons for this which all relate to concerns potentially limiting the applicability of the evidence (population characteristics, aspects of intervention described, the setting) to the review topic and the population of interest as specified in the review protocol. In recognition that the views of people with ME/CFS who had experienced the interventions was important, this qualitative review was done with an accompanying call for evidence which allowed registered stakeholders to submit information relating to the review question. Evidence submitted within this call for evidence was assessed for inclusion in the evidence review in addition to the evidence identified in the systematic searches following the same process of assessment against the review protocol. All evidence identified through the call for evidence and the systematic searches has been assessed for eligibility, but we have not been able to consider evidence not identified through either of those sources. Cochrane reviews identified through the systematic searchers have been assessed for inclusion in the evidence reviews. For review G, we were not able to include potentially relevant Cochrane reviews identified due to differences in the review protocols and methodologies (for details on this see section 1.1.3.2 Excluded studies in Evidence review G) Included studies identified through the call for evidence also

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				of ME/CFS or understand the range of experiences. Interpretation should be applied with caution. We are concerned that not all are UK based, quantitative studies have not been appraised and a Cochrane review has also been dismissed as relevant evidence. The reporting of studies is inconsistent with much research deemed to have 'serious population indirectness, not having PEM as a compulsory feature and because of the lack of blinding in the studies. The draft guideline appears informed by qualitative studies with high risk of selection bias, without the rigor applied to the excluded studies. The Forward ME survey (2019) review along with other surveys included as evidence, seems to have greatly influenced the exclusion of other research and the direction of the draft guideline. BACME agree that the underlying mechanisms of the illness continue to need greater elucidation. However, there is evidence and increasing agreement as to the range of physiological changes, and ME/CFS being a systemic disorder with neuro-immune involvement. The draft guideline does little to reinforce this despite evidence of autonomic dysfunction, immune and inflammatory responses and changes in the anaerobic threshold. Therefore, it would be more accurate, helpful to specialists and primary care, and validating for patients to indicate the body systems that are known to be involved. There is a growing body of evidence excluded and not considered by the committee on the HPA axis involvement, autonomic nervous system and immune system involvement and metabolic disorder. Health professionals need to have greater understanding of the dysregulation and systems affected by the illness. We are concerned this draft guideline does not give a full and accurate account of what is known about the condition and its development. There may not be a singular identifiable factor, common to all with the condition, but that is not the same as	included unpublished surveys such as the Forward ME Survey (2019). The inclusion of surveys identified through the call for evidence has not impacted the exclusion of other evidence as each study is assessed individually against the review protocol inclusion/exclusion criteria. The methodological limitations of these studies and our confidence in the findings emerging from them have been assessed in the same way using the GRADE CERQual approach. We agree there are important limitations in the evidence, that have been identified and accounted for in the assessment of confidence in the findings which is taken into account in decision making. The Forward ME survey 2019 has been downgraded for concerns over methodological limitations due to concerns over the recruitment strategy used, the data collection method (including open ended questions focusing on negative aspects of treatment) and concerns over data analysis as specified in the qualitative evidence table for the survey in Appendix D on Evidence review H. This has been accounted in the assessment of confidence of review findings that the survey contributes to. The limitations in the evidence have been brought to the committee's attention and taken into account in decision making and any conclusions emerging from the evidence have been interpreted with caution. In addition to this, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to and the indirectness rating of the quantitative findings and in turn on the overall assessment of confidence in the findings (qualitative data) and the quality assessment (quantitative data). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were

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				stating that we do not know or understand many of the physiological abnormalities. We are concerned that the draft NICE guidelines for CFS/ME do not accurately reflect the current research base, the experience of those working in specialist services or patients who have received specialist care. Our members frequently observe patients improving with the treatments offered and, whilst not everyone progresses beyond stability for many reasons also not represented by the review, some will make a good recovery. This draft guideline introduces unsubstantiated and outdated opinion, adds little new guidance and takes much away.	not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance/indirectness. See evidence review H Appendix G on PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed that in order for this criterion to be adequately met, self-reporting of PEM would not be sufficient and 95% of participants need to have been diagnosed by a health professional as having PEM. The Forward ME 2019 survey did not meet this criterion as 98.5% self-reported their experience of PEM. As a result, evidence from the survey was further downgraded for concerns over the applicability of the population, which is reflected in the relevance rating component of the assessment of confidence in the findings. This resulted in further downgrading the confidence in the relevant review finding from Moderate to Low quality. The committee agreed methodological shortcomings are important and this approach has been followed throughout the guideline to ensure such shortcomings have been accounted in the assessment of confidence in the evidence/evidence quality which contributes to decision making along with the variety of factors including the different types of evidence, the balance between benefits and harms, economic considerations, equality considerations and the committee's clinical expertise (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). A variety of different studies have been included in Evidence review G and across the evidence reviews, including various studies capturing the experience of people as well as that of care givers of people who have received care from specialist ME/CFS services. In addition, the importance of specialist services has been acknowledged throughout the recommendations made in the guideline and specialist services have specifically been

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					recommended as the key to successful management of ME/CFS. Information on the heterogeneity of ME/CFS, has recurrently emerged across the qualitative evidence reviews and has been acknowledged in the recommendations made. Please note that Evidence review G was not the only source of information the committee considered when making recommendations; it was only part of the wide range of evidence that the committee considered, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee also used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendations.
BACME – British Association for CFS/ME professionals	Evidence Review H	015	Table entry 16	BACME are concerned to discover a potentially fundamental contradiction. The discounting of published research that applied the Fukuda criteria due to the claim that the key symptom of Post -Exertional Malaise (PEM) is not considered goes against the proposed new NICE criteria for diagnosis which does not include PEM.	Thank you for your comment. No study was excluded because recruitment did not include PEM as an essential criterion. The evidence was considered indirect and this was accounted for in the quality assessment of the evidence (See the Methods chapter for information on GRADE). After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants

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					with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.
BACME – British Association for CFS/ME professionals	Guideline	General	General	In response to this draft guideline, BACME has received written comments from 22 NHS CFS/ME services along with BACME board members having many lengthy conversations with colleagues working within NHS specialist CFS/ME services. BACME has several patient and carer representatives on our board who have also contributed to our collective response. The comments below therefore reflect the views of a large number of professionals with extensive experience of working in this field along with the voice of patients who have had positive experiences of NHS services and who invest a huge amount of personal time working to support the provision of, and advancement of, care for people with ME/CFS within the NHS.	Thank you for your comment.
BACME – British Association for CFS/ME professionals	Guideline	General	General	The following comments about the draft guideline have been submitted by the BACME executive trustee patient and carer representatives: As an organisation we welcome the opportunity to comment on the Draft Guidance and appreciate that its development has been a complex and demanding process. It is unfortunate from both the patient and practitioner point of view that the overall tone of the Draft Guidance is negative despite it containing some positive and constructive content. The Draft Guidance doesn't seem to promote, or support with any confidence or clarity what specialist ME/CFS Services provide. The ME/CFS Services deliver continually developing, informed, and evidence- based protocols and strategies that address specific rehabilitation and the best possible level of recovery for	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These

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				the individual concerned. People with ME/CFS are generally desperate for such intervention and they value what is provided from specialist multidisciplinary ME/CFS teams. While we accept that there is, currently, no pharmaceutical cure for the illness we would expect the patient from their first contact with health services to be given relevant and up to date information and a specific action plan as the starting point of their recovery pathway. People with ME/CFS need to be given hope that change in how the illness affects them can be made. To support the above, health- professionals need up-to-date training about the illness to initiate first steps in progress, facilitate early initial diagnosis and be confident in referring patients promptly to Specialist ME/CFS Services. Question 2: Increased funding is the key to improved patient outcome. There is need for- • Access anywhere in the country for all ages from child to elderly, with minimal waiting time, to specialist multidisciplinary ME/CFS Teams. • Appropriate intervention period for each person (patients regularly comment they want more sessions than can be provided) • Intervention for all levels of the illness, particularly for the very severe/severely ill and children and young people. • Ongoing Service development • Research, particularly biomedical. As with other long term illnesses people with ME/CFS need to be given the message from community care onwards that steps to wellness can be made and that there are dedicated professionals to support them on that path.	recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. ME/CFS specialist services The committee agree that ME/CFS specialist services are important in the care of people with ME/CFS and have recommended this throughout the guideline. A definition of a ME/CFS specialist term has been added to the terms used in this guideline. Training The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. *Funding* The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as access to specialist teams, to implement some recommendations in the guideline. However, this guideline highlights areas where

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					resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned.
BACME – British Association for CFS/ME professionals	Guideline	General	General	BACME members are concerned that the tone of this guideline has been heavily influenced by opinion rather than evidence. The pessimistic tone does not reflect the experience of specialists working in this field and we feel that it demonstrates that other patient voices have not been heard. There are many people with ME/CFS who have been supported by the primary health care professionals involved in their care and many people who have derived benefit from accessing an NHS specialist ME/CFS service. Question 3 examples of good practice: This is a small selection of patient feedback comments that services have contributed to demonstrate that a more positive outlook is appropriate for this guideline: • *"My experience from the point of referral has been fantastic and the Service has been outstanding in my care. The CFS Service communications were clear and timely, the Consultation process provided proper information about the condition, a diagnosis and confidence that I would receive the treatment I needed. Finally I cannot speak highly enough of my Specialist Occupational Therapist. She is an excellent, knowledgeable and patient centred therapist who not only provided me with the treatment programme, but was also incredibly caring and supportive*" • "*You have given me everything I need to continue to get better* " • *"I've made such progress and improvements in my health thanks to this service"*	Thank you for your comment and the information. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. Thank you for your response. We will pass this information to our local practice collection team. More information on local practice can be found here:

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				- *"I found that realising that I was not going mad and that I had an illness, really helped. Also, the coping strategies put in place have changed my life. Meeting others with the same illness and realising that I was not alone. I have accepted the fact that I have an illness which means I can have a good quality of life, even though it won't be the same lifestyle as before.* - *" You've enabled me to understand the CFS and guide me in being able to make a full recovery, there were times when I didn't think this would be possible"* - *"I now have the confidence to manage my condition and educate other people"* - *"Treatment with this service was led by my personal circumstances and symptoms (wasn't 'one size fits all') which allowed for the most improvement. I was accommodated when I couldn't come to the centre, as home visits were arranged and times were flexible. My specialist focussed on a range of methods and techniques for managing my symptoms instead of pushing for improvement, which I feel has really benefited me. There was no pressure to 'get better', only to find ways to help me manage my condition long term. My specialist was both incredibly knowledgeable and hugely sympathetic and supportive, which in my experience, aren't always found together in the medical profession! A truly fantastic service. I wish all people with CFS/ME could access it."* - *"It was such a relief to talk to people who understand the illness and the effects. The family day was really good for people to bring their loved ones who are struggling to understand this illness. I really did not believe that therapy was what I needed and didn't think*	https://www.nice.org.uk/localPractice/collection?page=1&pageSize=10&type=&published=&filter=ME+.

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				it would help but I was so wrong. Therapy with XXX has completely turned my life around after nearly 6 years of feeling I was just living in a cloudy existence. I didn't realise how much it had affected me mentally and emotionally and XXX unpicked all of that session by session. I now feel so much better, I know I will always have this illness but I am able to deal with it now. For any sufferers out there who feel hopeless, please keep going to the doctor and request an assessment with XXX. It has changed my life having therapy with XXX (even having most of it over the phone due to COVID wasn't an issue) XXX just absolutely knew how to unpick my unhealthy thought processes and gave me tools on how to manage my emotions better which has had such a positive impact on my physical health." • *"From the beginning, the service I have received from XXX has been excellent. Professional, humane, highly personalised and adaptable. It is clear that the specialists at the clinic really know the subject of CFS/ME. The initial assessment/planning sessions with X were helpful in themselves, I was able to start some useful practices straight away. I did try to access the group therapy, but was too unwell at the time, so X suggested seeing me at home; these visits have been of huge benefit. In every session, I learned something new about my condition and techniques for supporting or improving my quality of life – meditation, activity pacing, quality rest & sleep, improving nightmares, managing relapses and so much more. Ultimately, with his guidance, I am currently in remission and am confident that I will be able to support myself if my*	

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				symptoms return. If I need more support, I am also confident that I will be able to access the service again. Doesn't get much better than that!"	
BACME – British Association for CFS/ME professionals	Guideline	General	General	BACME are concerned that this guideline has not clearly acknowledged the uncertainties regarding therapeutic approaches to managing ME/CFS. The NHS England website features a document titled: Finding the Evidence: A key step in the information production process https://www.england.nhs.uk/publication/finding-the-evidence-a-key-step-in-the-information-production-process/ This is a direct quote from the section 'Acknowledging uncertainty': The source of evidence on health and care interventions in which errors or bias are least common is called the systematic review. If there is no systematic review on your topic, uncertainty exists. This uncertainty may be recorded in the Database of Uncertainties about the Effects of Treatments (DUETs) – this is a database of questions that patients and clinicians have asked, for which no systematic review can be found. Known uncertainties should be referred to in your information product. There should be no issue in reaching a consensus agreement with all parties involved that there is uncertainty regarding the most effective approaches to managing ME/CFS. We are concerned that this guideline makes no reference to this uncertainty regarding therapeutic approaches. Despite this guidance being in a draft format and under consultation, press releases have already been sent out indicating very direct statements about what therapies should not be provided to manage ME/CFS. Throughout this document there are many places where very dogmatic statements are	Thank you for your comment and information. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Uncertainties in the evidence are described in all of the evidence reviews and this is followed by the committee's discussion and interpretation of the evidence. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what

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				made regarding what should or shouldn't be provided with regard to managing ME/CFS despite the evidence review documents and expert testimonies very clearly demonstrating a lack of clear evidence base for this guidance. BACME requests that the NICE committee consider the scope of a guidance document regarding the ability to make any firm statements regarding management approaches in the absence of a robust evidence base. We also request that there is a very clear statement regarding this uncertainty. We also request that there is acknowledgement of the fact that effective and safe care can still be delivered by NHS clinicians who accept and work with these uncertainties so it is essential the NHS continues to fund specialist ME/CFS care.	the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
BACME – British Association for CFS/ME professionals	Guideline	General	General	We are some way off being certain about any therapy approaches in this condition. The press statement that NICE released may have stated that *'there is no 'one size fit's all' approach to managing symptoms*' but what has been heard is a message that people with ME/CFS should not be advised to grade up exercise and they should remain within an 'energy envelope'. This has given the medical profession and the public the impression that any person with a diagnostic label of ME/CFS should consider any form of gradual increase in exercise at any stage of their condition harmful and should be avoided. Can we ask the committee if this was their intended outcome? Services are already reporting harm caused by this public statement as it has undermined patient's trust in NHS services and caused them to question whether they should resign themselves to never being able to exercise again and accept that they will never be able to make progress. The press statement acknowledges that this guidance has been issued based on the opinion of the committee and awareness	Thank you for your comment and information. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of

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				that some people have reported harms from a GET programme. There is therefore acknowledgement that this statement is not based on any published evidence and nor is it based on the opinion of the vast majority of clinicians who work in NHS services, nor is it based on the opinion of patients who report positive improvements in their health as a result of following a supervised, individualised graded activity program. The BACME National Services survey data and feedback BACME have received from our members in response to this document, demonstrates that many of the NHS specialist CFS/ME services that have continued to use the term GET to describe their therapy programmes, have adapted the approaches to fit with a dysregulation model of understanding the illness. They have therefore applied it in a flexible and individualised way and ensured that patients are first provided with information on how to achieve stability with supervised follow-up to agree when would be a safe point to experiment with grading up activity. Through using these adapted approaches services have seen a significant proportion of people with ME/CFS able to gradually increase their activity levels and consequently improve their overall physical and emotional wellbeing. Services have also combined many other therapeutic processes to explore what strategies and approaches may be helpful for this very heterogeneous group of patients. BACME ask the committee to reflect on the potential harm caused by producing inflexible guidance that dictates what therapeutic approaches should or shouldn't be used for a condition which has very complex physiological changes at its core and by its very nature is diverse and variable. While we are still gathering our understanding of this condition and to allow services to adapt to individual patients' needs and the evolving	the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility

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				evidence base, this guideline should allow for flexible approaches within a safe framework of monitoring.	• feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
BACME – British Association for CFS/ME professionals	Guideline	General	General	It is acknowledged throughout this document that there is a potential for people with ME/CFS to experience iatrogenic harm. Much of this harm occurs outside of specialist CFS/ME services because of a lack of understanding of what the condition is. The most effective way to establish patient safety regarding the delivery of care within specialist CFS/ME services, is to ensure services have robust processes in place to monitor outcomes and patient feedback. The BACME services survey explored this question and our report is available to download from the BACME website: BACME CFS/ME National Services Survey. Our survey demonstrated that the majority of services are already engaged in some form of outcome monitoring. However, services reported difficulties due to lack of standardised procedures along with lack of resources, time, and administrative support to enable them to do this effectively. Our survey report also highlights the importance of ensuring that outcome measures are meaningful for patients and acknowledges the potential burden on patients to complete them. There is consensus from all the services that have submitted comments to BACME that therapy programmes for people with ME/CFS should be multifaceted, flexible, patient focused, collaborative and individualised. This approach by its very nature	Thank you for your comment and information. The committee agree and throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. *Audit/outcome data* The committee agree that collecting outcome data and audit is an important part of measuring performance in services but this guideline focused on clinical recommendations, the development of audit systems was not included as an area in the scope and the committee are unable to make recommendations in this area. Your comments will also be considered by NICE where relevant support activity is being planned.

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				cannot be studied in a formal randomised blinded trial setting where the requirement is to deliver a standardised product. Question 2: It is therefore imperative that this guideline includes acknowledgement of the importance of services collating outcome data and recognition of the additional investment in services required to ensure this aspect of patient safety is prioritised. Question 3 re existing resources: specialists in this field have already done work on developing Patient Reported Outcome Measures and Therapist Reported Outcome Measures and BACME would be willing to contribute to the wider exploration of what form of outcome measures would be appropriate to use in a clinical setting.	. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
BACME – British Association for CFS/ME professionals	Guideline	004	005	Stating that 'the pathophysiology is unclear' leaves open the option that there isn't any pathophysiology and therefore that the illness isn't real. This is the starting point for the lack of belief, empathy and compassion that so many patients report experiencing during healthcare interactions from clinicians working outside specialist services. The guideline acknowledges this lack of belief and the prejudice and stigma that results from it on page 4 line 16 and also in the rationale section on page 47 line 13. This statement could also be used to imply that ME/CFS is a 'medically unexplained condition' and therefore lead to patients being referred to Medically Unexplained Symptoms clinics rather than specialist ME/CFS services. Specialist ME/CFS services provide explanations to patients regarding the possible processes generating their symptoms while also acknowledging that further research is needed to clarify the condition further. BACME therefore requests that this opening statement is changed to prevent further harm being caused by unhelpful attitudes towards the condition which come about because of people not believing it is real.	Thank you for your comment. The committee agree that it is important to have raise awareness and have clear statements about the reality and seriousness of ME/CFS. As you note the recommendations in the principles for care section do this, the first recommendation states the reality and seriousness of ME/CFS as a medical condition. The second recommendation acknowledges that people with ME/CFS have experienced disbelief and stigma. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed to edit 'unclear' to ,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and

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					support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.
BACME – British Association for CFS/ME professionals	Guideline	004	005	Stating that the 'pathophysiology is unclear' does not reflect the research advancements that have been made in this field. Use of the word 'unclear' implies there are only two states of knowledge- clear and unclear. The reality for all medical conditions is that there is a continuing evolution of knowledge and understanding and therefore all conditions are in a process of being clarified. A lot of research has been published demonstrating a variety of different abnormalities in people with ME/CFS which are generally considered to represent dysregulation in multiple dynamic systems in the body that are required to maintain homeostasis. The dynamic nature of the illness and the fact it affects physiological systems which are constantly changing, means the abnormalities are not demonstrated on standard blood tests and scans. BACME represents clinicians working in this field and we would request that the committee provides a more accurate and detailed statement regarding the recognition of physiological abnormalities particularly those demonstrated in the Autonomic Nervous System and Immune System along with the metabolic changes that have been established. The Yorkshire Fatigue Clinic has produced a referenced document presenting a model of Dysregulation as a way of understanding the illness available from the YFC website : http://www.yorkshirefatigueclinic.co.uk/media/uploads/2020/10/26/theory-model-oct-2020-95446.pdf BACME has shared this model with our membership and feedback from clinicians working in the field indicated that the majority of services are already using this model or something	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed to edit 'unclear' to ,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. *Appendix 1_Children and Young People.* This text is the background to the report written by the Oxford Clinical Allied Technology and Trial services Unit commissioned to undertake this project.

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				similar as a way of understanding the condition and explaining it to patients. In the Supporting Documentation – Children and Young people Appendix 1 page 8 line 5 states: 'Myalgic encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) are serious and chronic, debilitating conditions characterised by immune, neurological and cognitive impairment, sleep abnormalities, and autonomic dysfunction, resulting in significant functional impairment accompanied by a pathological level of fatigue.' We would expect that as a minimum a statement along these lines is included in the final guideline to acknowledge these physiological abnormalities.	
BACME – British Association for CFS/ME professionals	Guideline	004	010	In addition to the statement acknowledging that it can affect each person differently, it would be helpful for the guideline to acknowledge the heterogenicity of the condition and the potential for there to be multiple different subsets under the umbrella term of ME/CFS. This is important for research both in terms of understanding the causes of ME/CFS and also for studying treatment for it as it is possible that different subgroups may respond differently to different approaches. It is also important for the commissioning of services as there can be variation across the country regarding how diagnostic criteria are used and which groups of patients specialist services are commissioned to provide therapy for.	Thank you for your comment. The variation in the impact of ME/CFS and the importance of personalised care is highlighted throughout the guideline and for this reason this hasn't been added to the recommendation.
BACME – British Association for CFS/ME professionals	Guideline	004	013	Our executive trustee patient representatives stress that when describing ME/CFS as a fluctuating condition the patient's base line is at a much lowered energy capacity than when they were in generally good health, with increased symptom effect at times of relapse. The person does not return to normal capability /wellness after such events. Our executive trustee patient	Thank you for your comment. The aim of the recommendation is to raise awareness that ME/CFS is a fluctuating condition in which a person's symptoms can change unpredictably and sometimes quickly. Further information on the range of fluctuations would not help to clarify the recommendation.

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				representatives are concerned the draft guideline does not make this clear.	
BACME – British Association for CFS/ME professionals	Guideline	005	012 - 014	Question 1 re impact on practice and Question 2 re cost: Please could the Committee clarify who might be responsible for this regular monitoring and review, given that GPs are often not confident in the management of ME/CFS? If it is to be undertaken in specialist services, we would need extra provision for the cost of providing this regular monitoring and review, bearing in mind the number of people living with ME/CFS in England. In common with the majority of long-term conditions, self-management support for ME/CFS as currently provided in many specialist services focusses on fostering the skills to self-manage, which includes the self-management of flares (or dips) and relapse. The patient gradually takes on these self-management roles as their skills develop over time. A specific review might then only be needed if the patient is unable to self-manage the specific problems which their current relapse is causing, or if the relapse is not improving in a timely manner.	Thank you for your comment. The management of ME/CFS section of the guideline includes energy management and as part of that the self-management of flare- ups and relapses. The committee agree it is important that people with ME/CFS have the tools and strategies to self-manage their symptoms. The review in primary care section of the guideline has further detail on reviews and who should do them and this link has been added here. The review proposed is for at least an annual review unless the person's circumstances (for example they are unable to self- manage) require more frequent reviews. This is in line with other long-term conditions. The committee recognise that GPs are often not confident in managing ME/CFS (See Evidence review B). They have recommended in the training for health and social care professionals section that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline.
BACME – British Association for CFS/ME professionals	Guideline	005	012	Our executive trustee patient representatives welcome the recommendation for regular monitoring reporting that this is very useful particularly in the first year of illness, and during relapse.	Thank you for your comment.
BACME – British Association for CFS/ME professionals	Guideline	005	015	Engagement Our executive trustee patient representatives are concerned that the draft guideline should explicitly advise that health professionals must not misinterpret a seeming lack of engagement caused by illness severity. It should also be recognised that it is reasonable for people to have difficulty accepting the diagnosis and the accompanying long-term changes and what these mean to lifestyle and hope for the future. Question 3: Our executive trustee patient representatives highlight the need for flexibility in contact methods and can	Thank you for your comment. This recommendation is supported by the evidence and the committee's experience. Some people with ME/CFS reported negative reactions from health and social care professionals when they did not want to follow the advice given (see Evidence review A, Appendices 1 and 2). The committee agreed it was important to make a recommendation supporting people's choices and involvement in their care.

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				provide the patient perspective to the development of the guidance for this area.	The committee agree that flexibility in accessing services is important to all people with ME/CFS and this is address in the access to care section of the guideline and in the care of people with severe and very severe ME/CFS. Thank you for your offer of support on information in contact methods.
BACME – British Association for CFS/ME professionals	Guideline	005	019	BACME have received feedback from several NHS children and young people's specialist CFS/ME services who felt that many aspects of this draft guideline do not correlate with their experiences of treating children and young people. BACME therefore recommends that the committee consider whether a separate guideline for Children and Young People is required or whether a specific section could be created within the current guideline to specifically address issues related to children and young people with ME/CFS. Our concerns are: • There is confusion throughout the document regarding the timescale and process of diagnosis which could be simplified if children and young people were considered separately to adults. • There is lack of recognition of diagnostic exclusions which would be different in children and young people compared to adults. • There is also no reference to co-morbidities which have different patterns of presentation in children and young people compared to adults. • Prognosis is considered to be better for children and young people and this has not been reflected clearly in the current document which portrays this condition as lifelong and untreatable. • Some therapy approaches are more or less suitable for children and young people and children and young people may respond differently so it is important that evidence relating to adults is not presumed to apply to the care of children and young people.	Thank you for your comment. The committee agree that children are not mini adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made including the management of symptoms, support in education, access needs and safeguarding. *Diagnosis.* Children and young people do have different recommendations to adults in the suspecting ME/CFS section of the guideline prior to diagnosis at 3 months. If ME/CFS is suspected at 4 weeks than the committee have recommended referral to paediatrician for further investigation and then to a ME/CFS specialist team at 3months if ME/CFS is still suspected at 3 months (*S*ee evidence review D- diagnosis). Differential and co-existing conditions are listed in Evidence review D *Prognosis* When developing the guideline the committee was mindful of the importance of developing a guideline for all severities of ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that

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				- There are additional factors for children and young people around education, care needs, safeguarding issues etc which are important to acknowledge. Question3 re examples of good practice: Specialist paediatric services take a holistic approach and work with the individual child or young person and their family to see what support/advice/activity management would be beneficial for them. Families have the contact details of professionals to seek further advice and for use if symptoms worsen.	some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders the committee agreed to edit the recommendations on long term outlook (see recommendation 1.6.4) and the following one on children and young people (see recommendation 1.6.5). Thank you for your response. We will pass this information to our local practice collection team. More information on local practice can be found here: https://www.nice.org.uk/localPractice/collection?page=1&pageSize=10&type=&published=&filter=ME+.
BACME – British Association for CFS/ME professionals	Guideline	005	020	Our executive trustee patient representatives support the draft guideline's emphasis on experiences of prejudice and disbelief often due to ignorance of the illness. Such attitudes must not affect access to appropriate referrals, therapy, treatment and education for children and young people. Question 3: Our executive trustee patient representatives are able to offer expertise from the patient perspective to support greater insight and reduction in the myths of the condition.	Thank you for your comment and information.
BACME – British Association for CFS/ME professionals	Guideline	006	004 - 005	In the clinical experience of clinicians working with children and young people with ME/CFS, children and young people are particularly good at accurately describing their symptoms. We would be concerned if a parent were talking on behalf of a young person unless the child was very young, or the child or young person very severely affected.	Thank you for your comment. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity
BACME – British Association for CFS/ME professionals	Guideline	006	007	BACME welcomes the recognition of the impact of severe ME/CFS, however the placement of this section early in the document could cause confusion, distress to people with mild to moderate ME/CFS and undermines the experience of people with mild-moderate ME/CFS. This section lists many different symptoms of severe ME/CFS, and this appears ahead of the diagnostic section of the guideline. This gives the impression that the symptoms listed are unique to severe ME/CFS when in fact the symptoms listed are commonly present in all severities of the illness.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS.

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				We have had feedback from patients with moderate ME/CFS who read this and felt that it devalidated their experience of the illness. A person awaiting assessment who has had mild symptoms for a short period of time could feel distressed at the expectation that they will progress to this level of severity. We would recommend a more general statement at this stage in the document acknowledging that the severity of the condition can vary both over the course of time and in different people with consideration given to how different degrees of severity could be measured if this is felt important in terms of the level of care that needs to be provided by specialist services and community and social care services. BACME would support provision of specialist assessment and treatment for people with all severities of the illness. It should be acknowledged that it is only a small proportion of people with ME/CFS who develop a severe form of the condition and that prognosis may be different for different severities. It may be more helpful to feature a specific section further on in the guideline focusing on identifying and managing severe ME/CFS given that the needs for this group can be significantly different and more complex than those with mild to moderate ME/CFS. It would also be helpful to acknowledge the high incidence of co-morbidities in people with severe ME/CFS which adds to the complexity of their treatment and care.	Taking into account the range of stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. **Prognosis** After considering the range of stakeholder comments on long term outlook, recommendation 1.6.4 has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	006	007	Our executive trustee patient representatives welcome the focus on the severe/very severely affected patients and stress the need for insight into the level of cognitive and visual difficulties and support needed in communication methods. They also stress understanding that for those mildly affected our executive trustee patient representatives report much feedback that this group are particularly vulnerable to dropping into the Moderate classification.	Thank you for your comment and information. Taking into account the range of stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.

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				Question 3: Our executive trustee patient representatives can inform a more detailed account of the experiences and needs of this patient presentation which is currently too limited; and recommend an agreed protocol to ensure appropriate interaction. Severe/very severe sections need to follow on from mild and moderate in the guideline.	The point you raise about communication is addressed in this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. Thank you for your offer of support.
BACME – British Association for CFS/ME professionals	Guideline	006	007	Question 3 re existing resources: BACME have produced a detailed document on severe ME/CFS which was based on shared clinical practice and could be a useful resource to signpost people to when supporting someone with severe ME/CFS. Available from the BACME website: Severe CFS/ME: BACME shared clinical practice	Thank you for your comment. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
BACME – British Association for CFS/ME professionals	Guideline	006	014	Hypersensitivity to taste can also occur and is worth including due to its potential impact on nutritional issues.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
BACME – British Association for CFS/ME professionals	Guideline	006	022	The gastrointestinal and dietary issues that can arise in people with severe ME/CFS can be very serious and at times life threatening. It can be difficult to access appropriate help for this aspect of the condition so it would be helpful if there could be more emphasis on the seriousness of these symptoms and acknowledgement that in some cases it can lead to someone not being able to maintain adequate oral nutritional and may need specialist nutritional support including hospital admission and/or enteral feeding. Question 1 re challenging to implement for services and Question 2 re cost: Access to specialist dieticians who have an understanding of ME/CFS is extremely poor in the NHS and more emphasis could be given to the importance of dietician input early in the management of the condition to prevent more serious complications developing.	Thank you for your comments. The committee agree that all people with severe and very severe ME/CFS are at risk of serious gastrointestinal and dietary issues and recommend an assessment by a dietician with a special interest in ME/CFS. Enteral feeding is included in the examples of advice that could be given to people with ME/CFS. The list is not meant to be an exhaustive list. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.

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BACME – British Association for CFS/ME professionals	Guideline	008	001	Many services have provided feedback to BACME regarding the diagnostic section of the guideline. One of the primary comments regarding this section is that it is confusing especially regarding the numerous different timescales used which are different to other diagnostic criteria currently in use. If specialists with extensive experience of working in this field find it confusing and difficult to follow, then it is likely that health professionals outside specialist services will find it even harder to use.	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted that the advice recommended at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted. As you note this combination of symptoms cannot be considered normal and should be investigated but the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	008	001	Suspecting ME/CFS – use of this title for the diagnostic section puts too strong an emphasis on making a diagnosis of ME/CFS before considering other possible causes of fatigue. It is also confusing to have a section titled 'Suspecting ME/CFS' where the diagnostic criteria are listed and then a separate section titled 'Diagnosis' which seems to be solely based on the passage of time rather than clinical features. We would recommend using a title reflecting that the starting point is investigating the cause of fatigue symptoms while also providing some initial advice on	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the evidence reviews D and E.

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				management This can be done without using a diagnostic label of ME/CFS. The diagnostic criteria should be clearly labelled as a diagnostic section of the guideline.	*Suspecting ME/CFS* The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. The committee note the evidence on advice was lacking but that the advice recommended in the guideline at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted. As you note the symptoms should be investigated for other causes and the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • It is clear in the diagnosis section that diagnosis is dependent on the criteria persisting for 3 months and other conditions have been excluded.
BACME – British Association for CFS/ME professionals	Guideline	008	011	This guideline is recommending that ME/CFS should be considered as a diagnosis when symptoms have been present for 6 weeks in adults and 4 weeks in children. On page 49 line 18 the committee acknowledge that this recommendation is based purely on their opinion, not any published evidence base which also means there is no proof that it is a safe recommendation. This reduction in timescale for diagnosis to 4-6weeks has caused	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may

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				a huge amount of concern from the professional community for a number of reasons:
				• Risk of misdiagnosis: Time is a very important diagnostic tool in primary care and there are many conditions with symptom overlap with ME/CFS which may develop over several months e.g. coeliac disease, autoimmune conditions, lymphoma, diabetic autoneuropathy, B12 deficiency, endocrine disorders including Addison's disease, pituitary disorders, thyroid and parathyroid disorders etc. These conditions may present initially with fatigue and other symptoms which are seen in ME/CFS and the identifying symptoms or blood abnormalities may not show up in the early stages of illness. A diagnosis of ME/CFS often signals the end of the investigative process so indicating this diagnostic label should be considered so early could have serious consequences regarding delayed diagnosis of conditions which require specific treatment.
				• Risk of overdiagnosis: There are many acute illnesses that cause fatigue that take longer than 4-6weeks to improve, but full recovery will still occur – post-viral fatigue being a key one. It is routine for people to need 2-3months off work following major surgery. A significant bereavement could impact on someone's health and wellbeing long beyond a 4-6week timescale. One of the major problems with managing post-illness fatigue is people's impatience to get better and return to work and exercise. Reducing the timescale for diagnosing ME/CFS undermines the efforts to promote the need for time and patience to allow appropriate convalescence after an illness as it implies that having fatigue 4-6weeks after an infection, operation or
					prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion.
					
					However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are:
					• 'Provisional' diagnosis has been deleted for the following reasons:
					  o The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months.
					  o The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis.
					• Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
					
					Increased demand on services

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				emotional trauma is atypical and constitutes them having a serious lifelong illness for which there is no cure. - Psychological harm to patients: This guideline provides a very negative prognosis for people with ME/CFS stating it is a complex long-term condition for which there is no cure and no effective treatments. To deliver this diagnosis to a child who has only had symptoms for 4 weeks or an adult who has been unwell for 6 weeks could be devastating and could significantly hinder their recovery and impact very negatively on their mood. - Difficulty retracting the diagnosis: Many services report experiences of a difficulty in removing a diagnostic label of ME/CFS even if other causes for the symptoms are later identified. - Risk of increased demand on specialist CFS/ME services and paediatric services to provide assessments for people who may not have ME/CFS. Clinicians working in this field are well aware of the problems caused by the delay in making a diagnosis of ME/CFS however it is a gross oversimplification to assume that this can be solved by reducing the minimum symptom duration for diagnosis. ME/CFS is a condition with a large number of symptoms affecting multiple organs and systems in the body and therefore the presentation is complex and often requires a wide array of investigations to ensure other causes of the symptoms are not missed. It would be helpful for patients to be provided with fatigue management advice during this process of investigation, but we would advise that this should be done without using a diagnostic label of ME/CFS at such an early stage. Clinicians have expressed the importance of a timely and accurate diagnosis rather than an early one.	The diagnostic criteria are slightly stricter than in the previous guideline, although the duration of symptoms in adults has been reduced by one month to be consistent with children. Since the committee have now removed reference to a provisional diagnosis and made recommendations about testing for alternative conditions, the demand on services should not be so great. The committee agree that a timely and accurate diagnosis is important and have edited recommendation 1.1.4 to reflect this.

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BACME – British Association for CFS/ME professionals	Guideline	008	016	The statement 'symptoms are new and had a specific onset' fails to acknowledge the significant cohort of people who develop symptoms gradually sometimes over months or even years.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
BACME – British Association for CFS/ME professionals	Guideline	008	017	BACME are concerned that this guideline does not list the symptom Post-Exertional Malaise which has become internationally accepted as the key symptom to indicate the possibility of ME/CFS. It is not clear from the guidance why the committee felt this was an appropriate change to the Institute of Medicine's criteria that they have based the diagnostic criteria on. Change to use of the terms 'fatiguability' and 'post-exertional symptom exacerbation' could have several negative consequences: • Confusion: Fatiguability is a clinical examination finding in neurological practice which is not how the term is being used in this setting. • Undermining the validity of the illness: Post-exertional Malaise is a term which has been in use for many years and has been used in education and training settings both within specialist services and also in wider healthcare settings such as primary care. Removing this as a key symptom could serve to play down the severity of the fatigue that people with ME/CFS experience as it removes the recognition of it as a symptom that is	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms and hope this has added some clarity for readers • *Debilitating fatigability.* This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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				different to the normal experiences of fatigue that healthy people experience. • Capturing a different cohort of patients which could increase the number of people diagnosed with ME/CFS: The term malaise refers to immune mediated symptoms so without this symptom being required for diagnosis the cohort of people diagnosed with ME/CFS could include those with no immune mediated symptoms e.g. people with primary dysautonomias such as POTS. • Harder to understand: the language and layout used in the diagnostic box doesn't identify a clear symptom in the way that Post-exertional Malaise does. • Inconsistency: There is a NICE Clinical Knowledge Summary on Tiredness and fatigue in adults updated in March 2020 which includes a page on diagnosing CFS where the diagnostic criteria are different to those listed on this document including use of the term Post-exertional Malaise https://cks.nice.org.uk/topics/tiredness-fatigue-in-adults/ • International comparisons: It is hard to understand the rationale for the UK having a different list of symptoms for this condition compared to other countries.	
BACME – British Association for CFS/ME professionals	Guideline	008	017	The listing of sleep symptoms is confusing. Unrefreshing sleep is a symptom in its own right but this has been confused by then listing several other different sleep symptoms as if they are indicators of unrefreshing sleep. Many people with ME/CFS report having a normal night's sleep but wake feeling unrefreshed. Sleep changes such as broken sleep and hypersomnia can also occur but should be listed as separate symptoms. Hypersomnia could be an indicator of a primary sleep disorder so care should be taken when listing this as a key diagnostic indicator for ME/CFS.	Thank you for your comments. After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee hope this has added some clarity for readers.

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BACME – British Association for CFS/ME professionals	Guideline	009	004	The committee have based the diagnostic criteria on the Institute of Medicines Criteria which lists Orthostatic Intolerance as one of the key symptoms. It is not clear why the committee have felt it appropriate to downgrade this symptom. The rationale provided on page 64 line 21 is that the symptoms of orthostatic intolerance can be hard to differentiate from other ME/CFS symptoms. The symptoms of orthostatic intolerance are easy to identify as it requires simply asking a patient about what happens when they stand still. It is extremely common for patients with ME/CFS to report escalation in fatigue, pain and feeling lightheaded, faint or dizzy in response to standing. There are orthostatic symptom scoring systems available if a more detailed quantitative analysis is needed. It can be very validating for a clinician to be aware of this symptom pattern, to ask patients about it and be able to provide an explanation of why it happens. There are also specific strategies that can be used to help this aspect of symptoms Therefore to downgrade the relevance of this symptom is detrimental to patient care and fails to recognise the expertise that exists within specialist services where this aspect of history taking is becoming commonplace.	Thank you for your comment. The decision not to include orthostatic intolerance as a key criteria was not based on the rationale is that the symptoms of orthostatic intolerance can be hard to differentiate from other ME/CFS symptoms and this has been edited to make this clearer. The decision was based on the evidence of the criteria reviewed in evidence review D . They note that orthostatic intolerance is only described in 4 of the 9 criteria compared to cognitive difficulties that is described in 7 out of the 9 criteria reviewed. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
BACME – British Association for CFS/ME professionals	Guideline	009	009	Symptoms of twitching and myoclonic jerks are not common in people with mild and moderate ME/CFS and their presence would raise concern about an alternative neurological diagnosis and therefore caution should be exercised regarding listing this as a key symptom of ME/CFS.	Thank you for your comment. These have been removed.
BACME – British Association for CFS/ME professionals	Guideline	009	021	Question 1 re impact on specialist services: In contrast to the previous NICE guideline on ME/CFS, this guideline has not provided any guidance on investigations and the current statements could potentially be interpreted as saying no investigations are required. Many services have expressed concern about this omission and have requested that as a minimum a recommendation of blood tests is provided. Some of the problems caused by not having guidance on investigation are:	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the

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				- Many services are therapist led with no medical input and without a standard list of tests provided it can be difficult for them to ensure that patients have been investigated appropriately by their GP prior to making a diagnosis and referral to a specialist service. - Many services that have medical input do not have any access to investigations and therefore require all investigations to be performed in primary care prior to referral. - It would be helpful for parents advocating for children and young people presenting with fatigue to be able to request that an appropriate minimum set of investigations are performed. - It is common for services to receive referrals for people who have abnormalities on their blood tests which have not been investigated appropriately and services spend a lot of time contacting GPs regarding outstanding or abnormal tests - BACME therefore requests that further clarity is provided regarding the process of investigation for people with suspected ME/CFS including where the responsibility lies between primary and secondary care regarding performing the investigations. The committee could consider using the NICE Clinical Knowledge Summary on tiredness and fatigue which was updated in March 2020: https://cks.nice.org.uk/topics/tiredness-fatigue-in-adults/	importance of using clinical judgment when deciding on additional investigations.
BACME – British Association for CFS/ME professionals	Guideline	009	021	The committee have made the decision to base the diagnostic criteria on the Institute of Medicine criteria despite giving it an overall rating of 'Serious Limitations' in the evidence review. One of the key concerns for clinicians regarding the use of these criteria is that it does not include any guidance regarding	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. Taking into consideration the stakeholder comments the

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				exclusion criteria for diagnosis and we are concerned that this guideline has made no reference to potential 'red flag' symptoms that require further evaluation, other conditions that would constitute an exclusion to a diagnosis of ME/CFS along with recognition of common co-existing conditions. BACME therefore requests that further information is added to cover these omissions. There should be guidance on recognising indicators of conditions or situations which would warrant further investigation and different management approaches including: • primary sleep disorders including obstructive sleep apnoea • inflammatory joint conditions and symptomatic generalised hypermobility • Coeliac disease • Endocrine disorders • cardio-respiratory disease • untreated infections including Lyme Disease • primary mood disorders including PTSD, depression, anxiety and OCD • primary dysautonomia conditions and autonomic neuropathy • focal neurological signs or symptoms • significant weight changes • medication issues e.g. long-term/high dose opiates	committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.' The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS and includes the examples you have listed.
BACME – British Association for CFS/ME professionals	Guideline	009	021	The diagnostic criteria used for this guideline does not provide any acknowledgement or guidance regarding overlapping conditions which can present with a similar pattern of symptoms to ME/CFS. There are many conditions where it is increasingly being recognised that fatigue can be a key symptom, often with a post-exertional pattern similar to that seen in ME/CFS.	Thank you for your comment. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS and includes the examples you have listed.

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				Common overlapping conditions are: - Hypermobility conditions including Ehlers-Danlos Syndrome and Hypermobility Spectrum Disorder - Autism - Primary Dysautonomia e.g. POTS - Chronic pain conditions including Fibromyalgia - Rheumatological conditions including inflammatory joint conditions - Post-Lyme Disease - Anxiety disorders including PTSD - Mast Cell Activation Syndrome - Post-concussion syndrome It is possible that there are similar physiological abnormalities occurring in these conditions, but it is also possible that there are different mechanisms contributing to the symptom presentation which also means different therapy approaches may be required. Responses to therapy may also be different meaning outcome measures and prognosis will also be affected. It is therefore important to acknowledge this heterogenicity. Question 1 re impact on inclusion criteria for referral to specialist services: This is an aspect of care which results in inequality of access to care for patients as it is unclear whether specialist ME/CFS services should be seeing patients with these overlapping conditions and whether ME/CFS services have the appropriate skills and training and resources to manage them. Commissioners interpret this complex area in different ways meaning different services, and therefore different patients, have different funding decisions made resulting in inequality of access to care.	To note that throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses and to tailor management appropriately. Taking into consideration the stakeholder comments the committee have now included examples of investigations that might be carried out. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the, 'symptoms are not explained by another condition.' Question 1. The guideline provides recommendations on when to refer to ME/CFS specialist services for confirmation of the diagnosis and development of the care and support plan. Throughout the guideline the importance of including other specialists is reinforced. In the co-existing conditions section of the guideline the committee are clear that when managing coexisting conditions in people with ME/CFS, the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account. It was not within the committee's remit to make specific recommendations on service design and delivery. However, it is clear from some of the evidence collected in this guideline that existing services do not always serve people with ME/CFS optimally and hence the recommendations for a specialist ME/CFS team. The committee note that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to specialists, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments

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				Non-ME/CFS specialists can also make different decisions regarding the cause of a patients fatigue symptoms often labelling them as having ME/CFS when a specialist ME/CFS service would formulate their diagnosis around recognising their fatigue as part of their primary condition. Clarification is required regarding whether these conditions should constitute an exclusion to a diagnosis of ME/CFS and whether care should be provided in a specialist ME/CFS service. Question 1 re challenging to implement for CFS/ME services and other secondary care services along with Question 2 re cost: This could have significant implications regarding the volume and complexity of patients being referred to ME/CFS services and the skills and resources required by services to provide care to people with a wide spectrum of complex needs. It could also have implications for other NHS providers if the expectation is that they develop programs to provide fatigue management advice within other secondary care services.	will also be considered by NICE where relevant support activity is being planned.
BACME – British Association for CFS/ME professionals	Guideline	010	001	Question 1 re challenging to implement for primary and secondary care providers: The guideline states primary care professionals should seek advice from 'an appropriate specialist'. It is unclear what is meant by an 'appropriate specialist'. If this refers to specialists in ME/CFS services, then it needs to be acknowledged that there is not a recognised speciality and doctors working in this field come from a wide range of clinical backgrounds. This is shown in detail in the BACME National Services survey available from the BACME website: BACME CFS/ME National Services Survey It also needs to be acknowledged that a significant proportion of specialist ME/CFS services do not have any medical input and therefore GP's in those areas will not have an ME/CFS specialist doctor to seek advice from. This creates inequality of access to specialist care for patients.	Thank you for your comment. A description of ME/CFS specialist team has been added to the terms used in the guideline and further information has been added to the committee discussion in Evidence review I-multidisciplinary care. Medical input After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP

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				Question 2 re cost: BACME would support clarification from NICE regarding the expansion of specialist medical input for people with ME/CFS.	with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. Cost The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as the provision of medical assessment, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
BACME – British Association for CFS/ME professionals	Guideline	010	001	It is unclear from this statement whether the diagnosis of ME/CFS is expected to be made in primary care or in a secondary care specialist service. There have been published studies as well as CFS/ME service audit data demonstrating that the accuracy of diagnosis in primary care is low. GPs can vary significantly in their confidence in making a diagnosis of ME/CFS as the vast majority of GPs have received little or no training on the condition. Many clinicians conducting diagnostic assessments in specialist services report that around 50% of the patients they assess who were referred with suspected ME/CFS are found to have other causes for their fatigue. The process of conducting a detailed diagnostic assessment in a specialist services includes a consultation of at least an hour or more along with significant amounts of administration time spent looking through investigation results and secondary care correspondence. It is inappropriate to expect this to be conducted in primary care for patients with complex presentations. Not all specialist CFS/ME services currently provide a diagnostic service, especially those that operate without any medical input. Question 1 re specialist service delivery and Question 2 re cost: Therefore if this guideline is recommending that an ME/CFS specialist diagnostic assessment should be available then there	Thank you for your comment. The qualitative evidence and the committee experience reflect your comments about the lack of confidence in GPs in diagnosing ME/CFS, the high rates of different diagnoses and the complex assessments carried out by ME/CFS specialist centres. The committee agreed it was not clear in the recommendations about when a diagnosis is made and after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for a diagnosis for both the clinician 'provisionally diagnosing' and the person with the symptoms. • It has been clarified that if symptoms continue for 3 months then a person should be referred to a ME/CFS specialist team for confirmation of the diagnosis (this is adults is most likely from primary care and in children and young people they referral is from a paediatrician). It is at this point a detailed assessment is then recommended.

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				needs to be acknowledgement of the need for expansion of medical input into services, guidance on what specialities of Doctors should provide this service and the additional training and costs involved in providing it. Currently there is significant inequality across the country regarding access to specialist ME/CFS diagnostic assessments.	*Implementation costs* The committee agree there are areas that may need support and investment, such as training costs and access to ME/CFS specialist care, to implement some recommendations in the guideline. Your comments will also be considered by NICE where relevant support activity is being planned.
BACME – British Association for CFS/ME professionals	Guideline	010	003	Our executive trustee patient representatives support the referral to specialist support over an extended period. They emphasise from the patients they represent that there is evidence that such input is likely to generate some level of recovery. Question 1: The impact upon specialist service provision of increased referrals to disparate provision could be overwhelming. Question 2: Funding should be sufficient for rapid access to specialist ME/CFS Services for all ages in any part of the country. There is a major cost implication of sufficient funding across the ME/CFS specialist sector. Question 3: Our executive trustee patient representatives highlight how invaluable specialist ME/CFS Services are and will be able to collaborate with the committee to support the delivery of specialist interventions from the patient perspective.	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist. This recommendation relates to the provision of advice on symptoms to general practitioners. This advice could lead to fewer referrals.
BACME – British Association for CFS/ME professionals	Guideline	010	011	Advice for people with suspected ME/CFS- according to the proposed diagnostic process, this section is aimed at children and young people who have had symptoms for 4 weeks and adults who have had symptoms for 6weeks. The rationale for this section of the guidance provided on page 51 line 4 states there was limited clinical evidence on management strategies for people with suspected ME/CFS. If NICE's remit is to provide guidance based on evidence reviews and there is no evidence on which to base this guidance we would question whether it is appropriate for this section to be included without any acknowledgement of the lack of evidence behind the statements made.	Thank you for your comment. The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. This has been clarified in the discussion section.

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				When proposing a suspected diagnosis so early in an illness there is a possibility that people have as yet undiagnosed conditions for which the guidance given could cause harm.	The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. Taking into account the views of people with ME/CFS in the qualitative evidence the committee agreed it was important to make recommendations for support at this stage while acknowledging there is a lack of trial evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS. The committee agreed the advice would not be harmful in the short term either to people that are later diagnosed with ME/CFS or those that are diagnosed with another condition.
BACME – British Association for CFS/ME professionals	Guideline	010	011	This section is providing guidance on advice to be given to people who have had symptoms for a very short period of time and yet there is no acknowledgment of the fact many people at this stage will recover spontaneously. The purpose of including this section is in the hope that providing early advice will prevent a deterioration in symptoms and presumably improve the chances of recovery. The section should therefore use positive language that instils hope while also recognising the importance of regular review. It is possible to provide advice on managing fatigue without needing to use a diagnostic label at an inappropriately early stage of symptom development. Given that the rest of this guideline provides a very bleak prognostic impression with no hope of any effective treatments or cure then it is unhelpful and potentially detrimental to use a diagnostic label of ME/CFS at such an early stage of illness.	Thank you for your comment. The committee disagree the wording in this section is negative but after considering the stakeholder comments on early diagnostic labels the committee have amended the wording in the earlier section on suspecting ME/CFS to remove the recommendation on making a provisional diagnosis of ME/CFS. However the committee agreed it was important to provide advice for people with suspected ME/CFS at this stage recognising that some people may not be diagnosed with ME/CFS. The committee agreed the advice would not be harmful in the short term either to people that are later diagnosed with ME/CFS or those that are diagnosed with another condition. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and

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					edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
BACME – British Association for CFS/ME professionals	Guideline	010	015	Question 3 re existing resources: BACME has produced a patient guide to managing post-viral fatigue which is available from the BACME website and could be a useful document for GP's to signpost patients to. It also provides guidance on when to suspect ME/CFS. Post-viral fatigue: A guide to management	Thank you for your comment. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme..
BACME – British Association for CFS/ME professionals	Guideline	010	017	Use of the word 'perceive' in this statement is inappropriate and unhelpful. It could be interpreted as indicating the fatigue is not real and will therefore contribute to the lack of belief and understanding in health professionals that causes harm to patients. Advising people to not use more energy than they perceive they have is a subjective process and likely to be exceedingly difficult for the person with suspected ME/CFS and challenging for the professional advising them. This is particularly so for those people with ME/CFS who do not experience any "energy", and only experience the wide range of ME/CFS symptoms and the absence of energy. "Energy" may be a subjective sensation which is only experienced much later on for those who improve over time. Energy or fatigue levels are subjective markers and can be complicated by anxiety and fear of making symptoms worse so providing advice in this situation is far from simplistic as suggested by the few basic bullet points provided. This draft guideline recommends rest and staying within one's 'energy envelope'. The term 'energy envelope' is not widely used currently and therefore has the potential to be interpreted differently causing confusion.	Thank you for your comment. The committee disagree that the word 'perceive' implies that the fatigue is not real, perceive is clarified in the next part of the recommendation advising people to stay within this limit acknowledging the fatigue is real and individual to the person. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of trial evidence to support advice for people with suspected ME/CFS and this includes energy management. However the committee agreed the advice would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about managing their energy and how much rest is appropriate for the individual. *Energy envelope* After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and

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				While this can be a helpful short-term measure, in our collective professional experience, this advice limits progress in the medium to longer term. Inappropriate bedrest can be harmful, and a statement to this effect should be included as an ethical issue, with advice about how to manage the risks of bedrest, particularly for the severely affected. Advising people to stay within an energy envelope was not recommended in the last NICE guideline: where is the evidence to support this amended recommendation? We would welcome clarity on all of these issues, which have safety implications for people with ME/CFS.	information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. *Evidence review E* The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. This has been clarified in the discussion section. For further evidence and discussion on energy management see evidence review G-Non pharmacological management.
BACME – British Association for CFS/ME professionals	Guideline	010	020	We agree that rest is a vital aspect of managing ME/CFS, but we are concerned that the statement "to rest as they need to" might emphasise only reactive rest (increasing rest in response to increased symptoms) so we would also appreciate it if this section could emphasise planned rest, which involves "resting when they do NOT need to" in order to balance activity and rest in a sustainable pattern. We are concerned that the advice "to rest as they need to" does not address the need for pre-emptive rest in order to prevent post exertional symptoms, as explained in section 1.11.14. The section 1.11.4 is a much more helpful explanation of this approach: could some of this replace 1.3.1 Line 20?	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term before diagnosis. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with

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				As fatigue is often present all day every day, resting in response to fatigue could mean someone rests all day every day which could lead to secondary issues related to deconditioning and mood problems. The process of rest needs to be clarified as all types of activity can constitute a demand on energy systems. Many people would consider watching TV or reading as restful but when fatigue is present these activities may not provide good quality rest. If this section is retained in the final guideline, BACME would recommend that more detail is added to qualify what is meant by rest and the importance of taking regular structured rest periods throughout the day interspersed with periods of activity at a level which doesn't provoke an escalation in symptoms. It would also be helpful to include information regarding the potential for delayed exacerbation in symptoms as in the early stages many people have not recognised that their worse days are a consequence of doing too much on their better days.	ME/CFS may follow this advice and this would not cause harm to anyone. Section 1.12 recommendations on rest are for people that have been diagnosed with ME/CFS and as such are more detailed.
BACME – British Association for CFS/ME professionals	Guideline	011	015	A full history and holistic assessment are required before a diagnosis is made, not afterwards. Full assessment is necessary if alternative diagnoses are to be fully considered. It is not safe to diagnose any illness without undertaking a full history and holistic assessment first. Please amend the order of these two processes.	Thank you for your comment. The committee agree this is not clear and have revised the recommendation to, 'carry out and record a holistic assessment to confirm a diagnosis and inform the care and support plan.'.
BACME – British Association for CFS/ME professionals	Guideline	012	012	While the support measures included in this section can be helpful in the short term, there is no information included about strategies that facilitate progress in the medium to long term. It is our experience of working with children and young people with ME/CFS, that information given at the outset is pertinent and should include evidence-based information about possible recovery and about what supports recovery. The Guideline would benefit from clearer information about prognosis, stratified by age group rather than describing ME/CFS simply as "incurable".	Thank you for your comment. The committee have recommended that the care and support plan is reviewed at least 6 monthly for children and young people, this includes updating and revising strategies. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in

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					finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
BACME – British Association for CFS/ME professionals	Guideline	013	009	We thought that it would be helpful to have some examples of management plans so that the Guideline was more comprehensible. Our clinical experience is that the details of a management plan are developed gradually over a number of appointments, and that the details of a management plan might include a complex set of self-management skills which take time to develop. The guideline seems to suggest that a management plan might be written after the first assessment. In contrast to this rapidly produced document, the management plan for some individuals might develop into an extensive document. What did the Committee have in mind? Would an example of some management plans be helpful? Could it be an iterative plan, developed using shared decision making, including self-management principles? The BACME patient group suggest that any person specific management plan needs to be simple, specific, of personal use, and deliverable, acknowledging the significant time demands involved in developing a plan, and following it.	Thank you for your comment and information. This reflects the committee experience and more detail about the holistic assessment and development of the care and support plan has been added into the committee discussion in Evidence review I- Multidisciplinary care.
BACME – British Association for CFS/ME professionals	Guideline	013	012	Question 1 re challenging to implement for specialist services and Question 2 re cost: The guideline advises home visits should be provided by specialist services to people with severe ME/CFS. Currently not all services are commissioned to provide care to people with severe ME/CFS and even those services who	Thank you for your comment. *Home visits* The committee agreed that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be

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				do, not all of them have the capacity or funding to provide home visits. The BACME CFS/ME National Services Survey has data regarding this provision and is available from the BACME website: BACME CFS/ME National Services Survey The survey had responses from 42 UK CFS/ME services and 33% responded indicating they do not see people with severe ME/CFS. Out of the services that do see people with severe CFS/ME 43% do not offer home visiting. This means that BACME identified only 16 adult services across the whole of the UK who can provide the level of care to people with severe ME/CFS recommended in this guideline. The provision for children and young people is even worse with only 10 services identified that provide support to children and young people with severe ME/CFS. BACME supports increasing the provision of specialist care to people with severe CFS/ME and would welcome NICE highlighting this need while also acknowledging the costs involved in the required expansion of services and potential development of new services to have appropriate geographic coverage to provide equitable care across the UK. Home visits require more time, often involve multiple short visits, and travel expenses need to be budgeted for, so this work cannot come out of existing budgets for services. Please could the Committee recommend that additional funds are made available where required. Services that have not previously provided care to this group will require additional training. It may also be useful to reflect on the increased use of technology to provide remote consulting which could improve access to specialist advice for people with all levels of severity of ME/CFS. However, it is also important to recognise the demands and difficulties involved in both telephone and video calls for	difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. This recommendation is directed at assessment and development of the care and support plan. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the initial assessment and development of the care and support plan but for other consultations, other methods, such as online consultations, may be more appropriate depending on the person's symptoms. Implementation The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services for people with severe ME/CFS and training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				people with ME/CFS that may mean this type of healthcare interaction may not be suitable for someone with ME/CFS. People with severe ME/CFS may require home assessments regarding equipment and aids and due to the lack of provision of specialist ME/CFS services, this will currently be done by local community therapy teams. It would be helpful if this guideline could clarify the responsibility of specialist teams in light of the current low level of provision and how this access problem can be addressed.	
BACME – British Association for CFS/ME professionals	Guideline	013	012	The guideline makes no mention of the provision of specialist in-patient care for the management of ME/CFS. Currently there is very limited access to this in the UK and BACME would welcome acknowledgement from NICE regarding the provision of this level of care and what it should involve as this would aid commissioning decisions for patients being referred for this level of care.	Thank you for your comment. The committee agree that access to services for people with ME/CFS is very important and have reinforced this throughout the guideline. They agree there is variation in the delivery of some of the recommended services across the NHS including the provision of inpatient care for people with ME/CFS. The guideline addresses access to hospital care in the access to care section and also includes recommendations for people with severe or very severe ME/CFS. There was no evidence identified in any of the reviews on the provision of specialist inpatient care and the committee were not confident in making service delivery recommendations in this area.
BACME – British Association for CFS/ME professionals	Guideline	014	019	We would appreciate it if the Committee could review these comments regarding relapse and remission and make clear whether it is referring here to people with mild, moderate, or severe ME/CFS. We think that it is important to offer people with ME/CFS clear information about prognosis, and it would be helpful if the Committee could refine this advice further, stratified by severity. Our executive trustee patient representatives would like clarification on what is meant by remission. This should not be assumed to be back to normally well. Observation is that there can be some functioning at a more normal level for some time but if this is actually more than the person can really do, then this	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet points and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.

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				may result in a relapse and the need to re-establish stability over time.Recognition of the influence lifecycle changes such as menopause and events such as pregnancy, bereavement and other illness and trauma needs to be recognised treated as part of a relapse prevention plan. Question 3: Our executive trustee patient representatives stress more in-depth and specific guidance around how changes to lifestyle can promote improvement and recovery and will be able to work with the committee to contribute the patient perspective.	
BACME – British Association for CFS/ME professionals	Guideline	014	022	While ME/CFS varies in long-term outlook from person to person, there are usual timescales attached to different ages (adults differ from Children and Young People (CYP)) and according to severity. It would be helpful to include information about prognoses for different groups. Available data shows that many CYP diagnosed with ME/CFS recover. This was collected from NHS services using a national outcome database and is published. The statement 'although a small proportion of people recover' does not differentiate between children and young people compared to adults. This removes hope for young people and is not ethical as it is not based on evidence. The statement that 'the outlook is usually better in children and young people than in adults' does not indicate that, based on all available papers, significantly more than 50% recover, this means the majority of young people recover, which is significantly more than a 'small proportion'. Children and young people with ME/ CFS have a significantly higher rate of recovery when compared with adults' Carruthers, Van De Sande Mi, De Mierlier et al (2011) cited in Gregorowski, Simpson & Segal (2019). Reported recovery in young people is between 54 and 94% Crawley, E (2017). Young people have a mean duration of CFS of 5 years, with 68% reporting recovery by 10 years, Rowe (2019).	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your points: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
BACME – British Association for	Guideline	014	028	The statement regarding potential triggers for escalating symptoms includes childbirth. Many clinicians and patient representatives have responded to this stating in their clinical experience many women remain stable through childbirth and	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples as suggested in your comment were considered potentially

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CFS/ME professionals				some even improve so they are concerned that listing this could influence women's choices regarding having a family or could provoke unnecessary anxiety.	misleading information and not always a trigger and there are comments that gave other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	016	006 - 008	BACME would like to highlight that collaboration between ME/CFS experts and Safeguarding experts is recommended in complex situations where potential Safeguarding issues are being considered.	Thank you for your comment. The committee agree and have recommended that safeguarding assessments should be carried out by health and social care professionals who have training and experience in ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	017	008 - 019	Professionals working in children and young people's services voiced concerns with regard to parents / carers acting as an advocate on behalf of the child / young person by 'communicating on their behalf'. There is the real risk that the voice of the child or young person would likely be lost in this way. Sound adolescent health practice advocates the use of the HEADDSS Psychosocial assessment tool to allow the young person the space to talk about sensitive issues and for professionals to determine if there is psychosocial risk such as significantly low mood that needs addressing and this recommendation contradicts the earlier reference to hearing the 'voice of the child'. In addition, if a CYP was not brought to their appointment be it virtually / phone or in person, professionals would have to refer to their Trusts' 'was not bought' policy and consider safeguarding implications.	Thank you for your comment. The first section on principles of care includes a recommendation on ensuring the voice of the child or young person is heard. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity. The following recommendation in this section (1.7.5) is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.

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BACME – British Association for CFS/ME professionals	Guideline	018	010	Question 1 re challenging to implement for NHS services: Whilst we support the intent of this section, there could be a conflict between this advice as worded and the policies of many healthcare providers in the way in which repeated failed attendances are managed. These policies are in place to offer fair access to services for all patients, so that those who are waiting for an appointment are not disadvantaged by delays caused by multiple failed attendances. We suggest that the wording be changed to "Contact them in writing to offer them the opportunity to speak to a member of the clinical team to discuss the reason (s) why they were unable to attend, and to develop a plan to manage the risk of missed appointments."	Thank you for your comment. After considering the stakeholder comments the committee edited this recommendation to, 'If a person with ME/CFS misses an appointment: • do not discharge them for not attending because it could be due to their symptoms worsening • discuss why they could not attend and how the multidisciplinary team can support them' and hope this addresses your points.
BACME – British Association for CFS/ME professionals	Guideline	018	013	We welcome the addition of this section, which we think is helpful and important.	Thank you for your comment.
BACME – British Association for CFS/ME professionals	Guideline	021	006 - 007	Overall, this is a useful section, however the statement that 'some people find that going back to work, school or college worsens their symptoms' requires context to avoid it creating fear and preventing those able to return to school from doing so. It is our experience that many young people are able to return to school on a reduced timetable and choose to return to school as a goal.	Thank you for your comment. Recommendation 1.9.4 provides specific information on children and young people and discussing a flexible approach to training and education. Further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion.
BACME – British Association for CFS/ME professionals	Guideline	021	011	It is reasonable to offer to liaise on the person's behalf, but this section makes no mention of the option of empowering the individual to communicate with their employer themselves. Understanding one's health, the challenges associated with work and the potential solutions for these would enable the person to continue communicating effectively when they no longer have a clinician's regular support i.e. when they are self-managing.	Thank you for your comment. The committee agree that the issue of choice and personalised care is fundamental. Liaising with the employers, education providers and support services is in collaboration with the person with ME/CFS should only be done when appropriate and in the way that is best for the person.
BACME – British	Guideline	023	007	Question 2 re cost: We welcome this suggestion but note that this form of case management has resource implications, and we	Thank you for your comment. The committee agree that there is variation in the delivery of some of the recommended services

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Association for CFS/ME professionals				would welcome the Committee's comment about the provision of funding to cover this additional workload.	across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas.
BACME – British Association for CFS/ME professionals	Guideline	024	004	We agree that there is currently no evidence of a cure for ME/CFS but mention of prognosis at this stage would be helpful as otherwise the message is that it is "incurable". In contrast, it is a condition with an average duration. A clear definition of what is considered to be a "treatment" might be helpful here: there are multiple interpretations of this word. For example, some might consider support with pacing to be a "treatment": is the Committee suggesting that pacing, and other linked self-management approaches such as planning, and prioritising are not helpful? More clarity is required.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Earlier in the guideline in the information and support section the long-term outlook is described. To note, these recommendations have been slightly edited after considering stakeholder comments about the negative tone of the guideline.
BACME – British Association for CFS/ME professionals	Guideline	024	006	Our executive trustee patient representatives recommend viewing energy capability, rather than energy limits, as a continuum from lying in bed to ambulant. What can be maintained and developed at each level needs insightful and personalised assessment with planning for careful stages. They regard incremental activity development as acceptable if started from a definite maintainable base line when the patient is stable.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
BACME – British Association for CFS/ME professionals	Guideline	025	015	The wording as it stands is problematic because it focussed on minimising symptoms, not pacing. For many people with ME/CFS, bed rest might minimise symptoms in the short term. Is the Committee intending to recommend bed rest for so many people with ME/CFS? Taken literally, this would seem to be the case, but perhaps this is just the unintended consequence of this problematic wording? Would the Committee be willing to take full	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.

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				responsibility for any harm caused by this advice, if, taken literally, it leads to more patients becoming bedbound, with all of the potential harms which this can cause? There are cases where patients have followed such advice and have rapidly deteriorated. This advice as currently worded seems paternalistic in that it ignores the patient's own self-management decision making, which may be to choose a method of pacing which balances engagement with activities (which they can engage in to a limited extent) against symptoms which they may decide to accept in order to engage with these limited activities which are important to them. We think that the final decision about this balance of activity and rest should remain with the patient, respecting their autonomy, and not be decided by the NICE Guideline committee who are unable to consider all of the factors influencing each individual patient and their particular circumstances. We suggest that this section be refocussed upon finding sustainable levels of activity and rest, not a level which is purely focussed on minimising symptoms which risks all the harms of increased inactivity and disability. The first line (line 18) "reduce activity as the first step" should be removed as this is blanket advice which is not supported by any evidence, and which has not been informed by the individual assessment. It might be that the assessment finds that the patient is effectively pacing: why then advise a reduction in activity as the first step? We think that this section should be refocussed, bearing in mind the patient's own autonomy and self-management priorities.	
BACME – British Association for CFS/ME professionals	Guideline	025	025	It is common for a person with ME/CFS to experience a variation in symptoms during daily life, and during any movement, cognition and emotional expression required for function. We suspect that the Committee are NOT recommending that people only participate in activities which are symptom-free (i.e. do not "trigger" symptoms) but the current definition could be misinterpreted to mean this. We also think that the person themselves is best placed to take decisions regarding their	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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				activity levels, as they may have strong reasons to persist with some activities at times. We think that the use of the word flare (or dip) and also of a relapse are likely to be more helpful here, and the wording could be changed to: Discuss with the person with ME/CFS the potential benefits and problems associated with a self-managed reduction in their activity if their activity is at a level that frequently provokes a flare (or dip) or a relapse".	
BACME – British Association for CFS/ME professionals	Guideline	026	016 - 022	We welcome the inclusion of this section on physical maintenance.	Thank you for your comment.
BACME – British Association for CFS/ME professionals	Guideline	027	003	Question 1 re challenging to implement for specialist services and Question 2 re cost: We would like to see clarification around what is expected from specialist ME/CFS services and other HCPs individually. Many contacts are delivered remotely at the moment and likely might be going forward. How would this work? If clients can only tolerate for example, 5-10mins of specialist intervention, is this the best use of therapy time to be checking for pressure ulcers etc. Who is expected to do this and when? People living with severe ME/CFS may need additional care support from other agencies such as professional carers, district nurses etc. The responsibility to ensure factors such as pressure care are regularly monitored should perhaps be shared with or taken on by other professionals involved, especially if they have more frequent contact with the patient.	Thank you for your comment. Throughout the guideline personalised care is emphasised as part of the care and support plan, the delivery of care is specific to the person's priorities and needs. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. Service delivery is not within the remit of the committee and therefore they have not recommended in detail who should do what when. However, it is not anticipated that these checks will take long.
BACME – British Association for CFS/ME professionals	Guideline	027	024 onwards	We welcome the inclusion of this section recommending against these interventions as cures but would like to reiterate a concern that repeated reference to there not being a cure might be inadvertently harmful, given the variable prognosis of ME/CFS especially in younger people.	Thank you for your comment. *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any

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				We are concerned that the word "treatment" on page 28 line 1 has multiple meanings, and the use here may cause confusion. Treatment can mean "medical attention" which is a broad term, but the definition of treatment could also include rehabilitation treatments. The draft guideline supports the offer of a personalised physical maintenance plan, which BACME also supports: is this not a "treatment"? The draft guideline also supports the offer of a physical activity programme, which BACME also supports: is this not a "treatment"?	misinterpretation with the availability of treatments for symptom management for people with ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	028	012 - 015	We welcome this statement regarding physical activity.	Thank you for your comment.
BACME – British Association for CFS/ME professionals	Guideline	028	016 - 018	We welcome this statement regarding physical activity but would like to expand the list of healthcare professionals who can support the physical activity programme, provided they have training and expertise in ME/CFS. We think that mention of specific healthcare professions could be removed, or that physiotherapists and occupational therapists could be left as examples only. This section should not exclude the option of having support form a specialist GP or nurse, or a health psychologist with appropriate training.	Thank you for your comment. After considering the stakeholder comments the recommendation has been edited to ,'If a physical activity or exercise programme is offered, it should be overseen by a physiotherapist in a ME/CFS specialist team.'. This does not exclude the option of having support from a specialist GP or nurse, or a health psychologist with appropriate training but still ensures the person with ME/CFS still has input from a physiotherapist in a ME/CFS specialist team.
BACME – British Association for CFS/ME professionals	Guideline	028	025 - 026	We think that further clarity is required here. Line 25-26 states "establish their physical activity baseline at a level that does not worsen their symptoms. We think that the use of the word flare (or dip) and also of a relapse are likely to be more helpful here, as the aim should be to "establish their physical activity baseline at a level that does not provoke a flare (or dip) or a relapse". It is normal for a person with ME/CFS to experience a variation in symptoms during daily life, and during movement required for function. We do not think that the Committee are recommending that people only participate in activities which are symptom-free,	Thank you for your comment. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. This is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly. The final bullet point includes the recognition and management of a flare up or relapse.

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				as this would be impossible for many patients, but the current definition could be misinterpreted to mean this. We think that a reference which might evidence the role of specialist services would be: Crawley, E., S. M. Collin, P. D. White, K. Rimes, J. A. C. Sterne and M. T. May (2013). "Treatment outcome in adults with chronic fatigue syndrome: a prospective study in England based on the CFS/ME National Outcomes Database." QJM: monthly journal of the Association of Physicians 106(6): 555-565. This study clearly indicates the overall positive impact of specialist services, and (as is typical in NHS Services) 95% of those studied reported post-exertional malaise.	The committee agree and throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.
BACME – British Association for CFS/ME professionals	Guideline	029	017	The BACME patient group suggested that the advice on rest should be expanded, as the length, type and frequency will change as people progress with improvement. The wording of the Guideline at present suggests that the healthcare professional advises on how often and how long to rest, but we feel strongly that this should be a self-management decision, involving shared decision making.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. This advice would be part of the care and support plan that is developed by the ME/CFS specialist team and they are knowledgeable about the role of rest and sleep in people with ME/CFS and supporting them in making these decisions.
BACME – British	Guideline	029	017	Sleep	Thank you for your comment. *Sleep*

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Association for CFS/ME professionals				We are concerned to find that although unrefreshing, broken sleep and hypersomnia are outlined as symptoms that should be assessed, that sleep management is not addressed in the draft guideline, particularly when NICE are currently developing a technology related guidance for adults with difficulty sleeping GID-MT552 expected publication 3rd August 2021. Question 3 re existing resources: Current NICE Clinical Knowledge Summaries (CKS) for Insomnia both under and over 3 months were updated in 2020 and recommend good sleep hygiene should be established by addressing behavioural, environmental, and temporal factors. The need for information and resources is addressed in the guideline but we do not understand why recognised sleep management sources are not considered. NICE CKS recommend valid sources of materials can be sourced at MentalHealth.org.uk https://www.mentalhealth.org.uk/search?query=sleep https://www.nhs.uk/conditions/insomnia/ RCGP (2019) https://www.rcgp.org.uk/-/media/Insomnia-Top-Ten-Tips-v3.ashx?la=en. who refer to https://www.sleepfoundation.org/sleep-hygiene We regard the symptom of unrefreshing sleep as central to the condition. Evidence Review G includes sleep quality among the critical outcomes that matter most for decision making with unrefreshing sleep noted as a symptom. It is not referred to in the draft guideline. Disturbance to the Circadian rhythm is clearly recognised by specialists and would not be described as just 'light sleep' as the guideline suggests. Short-term memory loss and word finding difficulties are commonly reported and can relate to sleep disturbance. There is no account in the energy envelope theory of activities for poor sleep that can impact on symptoms or advice on how to	*Evidence review H, appendices* After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. *Evidence review E – strategies pre-diagnosis.* The beginning of the discussion section in Evidence review E states ,'the committee discussed this evidence with the findings from the reviews on Information for people with ME/CFS and their families and carers (report A), Information and Support for health and social care professionals (report B), access to care (report C), Diagnosis (D) non pharmacological management (report G) and the report on Children and Young people (Appendix 1). The committee took this evidence into account as well as their own experience and expertise. The committee discussion of this review sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. It is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice.

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				regulate sleep, one of several key components to consider when aiming to stabilise the condition. The Pre-Diagnosis Evidence review recommend advice regarding 'sleep habits'. This is not expanded upon which is a concerning omission to us. In Evidence Review E the Committee offer's its own view, rather than an evidence-base, suggesting that daytime sleep is beneficial in the early stages 'for some patients'. Specialists generally recommend gradually reducing daytime sleeping at the right pace for the individual. Increasing the quality of night-time sleep prompts the return of circadian rhythms, responsible for synchronising many body functions such as hormone release and appetite. Patient feedback is that if sleep is needed within the day as part of a structured rest-activity framework this improves quality of night time sleep. Trying not to take needed sleep increases pain and the 'wired and tired' state that acts against going to sleep. This is a different situation from people who are 'oversleeping' without need which can sometimes be related to mood problems. BACME stresses the need for an individualised approach to sleep management. Evidence review H, appendices, note sleep hygiene as a category but without any exploration or reference to any NHS guidance. It states the use of sleep management strategies as part of management of ME/CFS is widespread but variable. This section then goes on to claim that many services simply signpost or provide general tools. The basis for the statement seems more assumption than based on research or knowledge of specialist practice. We are very concerned that specialist knowledge and experience has not been sought to provide evidence for sleep	The committee agree that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline.

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				interventions, particularly when it appears Committee experience was used to outline rest techniques. Question 3: Our members have developed extensive skills in evaluating sleep issues and providing guidance on managing them. If it is beyond the scope of this guideline to provide this level of information, BACME will aim to improve provision of guidance on sleep issues based on clinician expertise.	
BACME – British Association for CFS/ME professionals	Guideline	031	006	'Do not offer any medicines or supplements to treat of cure ME/CFS'. This is an incredibly dogmatic and negative statement which could have wide reaching negative effects: • It could cause significant distress to a person with ME/CFS who will be made to feel there is no hope of ever having medications that help with the condition. • It is also contradictory to the statements that follow that imply that medications would be given to people, including children and young people, to manage the symptoms that occur in ME/CFS. • This statement will perpetuate unhelpful attitudes from doctors who often believe their primary role is to prescribe medication so without any requirement to do that for people with ME/CFS they will see that they have a minimal role in providing care for that person. • Given that this guideline could remain in place for many years, it is very dismissive of any potential progress in the understanding and treatment of the condition that may come through in future years. • It restricts research into potential drug treatments as it will perpetuate the situation where there are very few ME/CFS specialist clinicians who can oversee prescribing within a specialist service and therefore have the skills and capacity to be involved in medication based research.	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. As you note the discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.

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				BACME would recommend removing this statement and replacing it with something acknowledging that at the time of writing the guideline, there are no medications specifically licensed to treat ME/CFS, however there may be a role for prescribing common agents to help with managing some aspects of the symptoms that occur. Page 6 Line 7 of the Evidence Review F on Pharmacological Management has a more realistic statement acknowledging that medications are commonly used for people with ME/CFS and the tone of this statement should be reflected in the guideline.	
BACME – British Association for CFS/ME professionals	Guideline	031	006	The section on medication fails to acknowledge areas of clinical practice where progress has been made in the use of medications to improve symptom severity. The management of Dysautonomia, for some people, can include use of medications which lower heart rate and reduce the severity of orthostatic hypotension. Access to specialists who can prescribe these agents to people with ME/CFS is very poor and almost non-existent for children and young people. This is an area of treatment that could and should be expanded and recognition of these options should be included in this guideline with recommendations for expansion of access to these treatments. There should also be clarification about whether this should or could be done within specialist ME/CFS services if appropriate medical input and expertise is available. Equally the emerging knowledge about Mast Cell Activation Syndrome is another area where medications may be used to reduce the severity of symptoms experienced. Mast cell stabilising agents include over the counter antihistamines and H2 blockers which have clearly established safety records and therefore would pose minimal cost or risk if trialled in patients with symptoms suggestive of MCAS. Access to specialists who are able to formulate this diagnosis and advise on treatment is extremely limited in the NHS currently but there should be acknowledgement in this guideline that provision should be	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. As you note the discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.

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				increased and certainly within the lifetime of this guidance there should be the option for these treatments to be utilised more as research progresses our understanding. The lack of reference to these clinical areas in the guideline will restrict patient's access to treatments that may be of value to them.	
BACME – British Association for CFS/ME professionals	Guideline	031	007	Question 3 re existing resource: BACME has a Guide to Symptom Management available from our website: ME/CFS: Guide to Symptom management which includes pragmatic guidance for clinicians on the use of medications for people with ME/CFS.	Thank you for your comment. ' We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme.
BACME – British Association for CFS/ME professionals	Guideline	031	012	It would be helpful to add in a consideration of using liquid preparations of medications when available as this can allow more gradual dose adjustments and they often contain less excipients that can contribute to the medication sensitivities.	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
BACME – British Association for CFS/ME professionals	Guideline	031	014	Adding in the word 'slowly' would help to indicate that medication tolerance can develop if an appropriately low dose is used initially and increases are made below the level that provokes side effects. This needs to be adjusted on an individual basis according to symptoms and side effects rather than standard dosage regimes.	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
BACME – British Association for CFS/ME professionals	Guideline	033	004	Question 1 re challenging to implement due to lack of ME/CFS trained dieticians: There is a lack of specialist ME/CFS dietitians. We are concerned that the current wording may prevent people being referred to a dietician as they may not be 'specialist ME/CFS' dieticians and therefore deemed not appropriate according to NICE guidelines. We think it would be helpful to manage expectations about what is currently available, whilst including a clear aspiration to what would be best practice.	The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS'. This is because the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS

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					services. Special interest describes this group of professionals better. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. The re-wording might reduce the risk of increased waiting time but some areas might need to invest in training to implement this recommendation.
BACME – British Association for CFS/ME professionals	Guideline	034	001	This section does not reflect the evidence base especially regarding the provision of care for children and young people. There is considerable evidence from 5 RCTs that CBT for fatigue results in considerable improvement (wellbeing, quality of life and function) and recovery for > 60% and as many as 80% of young people with CFS/ME, including at longer term follow up. Therefore, to give the message that recovery is not expected seems to ill fit with the evidence base to date and will not instil hope or desire to change in young people. CBT for fatigue in the existing treatment trials has been effective in reducing fatigue substantially. We are not aware of any studies looking at the use of CBT for fatigue in young people that have not found a benefit, and none of the trials have raised major safety concerns. Most of these trials have excluded those with significant anxiety/depression (c.f. Loades, Sheils & Crawley, 2016; Stoll et al, 2017. We agree with the rest of the statements regarding the appropriate use of CBT approaches to support people with ME/CFS.	Thank you for your comment. After considering the range of stakeholder comments reflecting on the evidence the committee concluded that CBT could be offered to a child or young person with ME/CFs but only after they and their parents or carers have been fully informed about its aims and principles and any potential benefits and risks.
BACME – British Association for CFS/ME professionals	Guideline	035	019	The statement 'involve parents and carers in the therapy where possible' required clarification. We would hope that this is in relation to supporting the child or young person with the therapy rather than having a direct presence in the therapy sessions. It would not be suitable for parents to attend all the therapy sessions directly.	Thank you for your comment. After discussing this the committee noted that the involvement of parents or carers in therapy was usual practice but have edited the recommendation to, 'wherever possible and if appropriate.' For further clarification.

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BACME – British Association for CFS/ME professionals	Guideline	039	027 - 029	Question 2 re cost: offering children and young people with ME/CFS a review of their care and management plan at least every 6 months will have cost and resource implications.	Thank you for your comment. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. In the case of reviewing the care and support plan of children and young people, the committee agreed that there would potentially be long-term consequences associated with less frequent review, especially where the child's education was being adversely affected by their ME/CFS.
BACME – British Association for CFS/ME professionals	Guideline	040	007	Question 1 re resource limitations of specialist services: Ensuring reviews are carried out or overseen by a paediatrician with expertise in ME/CFS, involving other appropriate specialists as needed will be challenging to implement as there are not sufficient numbers of paediatricians with expertise in ME/CFS and specialist services are over stretched and require additional resource.	Thank you for your comment. The committee agreed that optimal care for children and young people with ME/CFS is provided by health and social care professionals that having training in ME/CFS. In particular a paediatric ME/CFS specialist team should confirm the diagnosis and develop the care and support plan. It follows from this that reviews are carried out or overseen by a paediatrician with expertise in ME/CFS. In evidence review I-Multidisciplinary care, the committee note that in particular children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres. A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.

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					The guideline reflects best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
BACME – British Association for CFS/ME professionals	Guideline	040	011	Training for health and social professionals Question 1 challenging for specialist services to provide training with current resources Question 2 cost implications to develop and deliver courses and for staff to be funded to attend: BACME agree that training for those who deliver care for people with ME/CFS will be helpful, particularly as the draft guideline implies that GP's should have the skills and knowledge to diagnose the condition. Our members raise the issue of GP disbelieving the existence of the condition. As this will take a lot of unpacking and engagement, BACME are concerned that the committee are not addressing this problem. Our members strongly advise supporting funding for clinicians in specialist services to access ongoing training. The BACME National Services Survey reports major shortfalls in continuing professional development with therapy staff rarely having access to a training budget adequate to cover the needs of working in this complex and evolving field. Diagnosis and care of a patient with ME/CFS is a partnership approach, and the draft guideline is already in danger of advocating for a 'do to' approach. Training must clarify such views are risky and adversarial and be able to promote equal collaboration. Insight and application of goal based approaches, mood, self-esteem, anxiety and hope for the future, self-efficacy and resilience would be required, and managing long term conditions.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs and access to ME/CFS specialist services, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be considered by NICE where relevant support activity is being planned. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in

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				BACME stress that the draft guideline does not clarify what the training should contain and who is to undertake it. The implication is that anyone delivering care should be trained to deliver the guideline. Professionals must understand ME/CFS is a complex condition with multiple symptoms and wide ranging impact. Drawing out the wide variety of symptoms takes skill and experience. BACME recommend levels of training applicable to the professional capacity and relationship to the patient. We are alarmed at the brevity of the section. The draft guideline does not detail whether training will include pre-registration and medical students and how the professionals be reached and engaged. Question 2: This recommendation is both unclear and concerning as there are no considerations of time the resources required, or cost accounted for. There is a large cost implication to competency based training for GP's and Primary care professionals which requires on-going monitoring. It is not made clear who will provide the training and at what level given the complexity, longevity and heterogeneity of patients' experiences. Specialist Services have limited capacity to manage their delivery of care at present. Some are able to offer AHP and medical student courses, however, to provide every practitioner across hospital, community and social care services who may come into contact with the condition requires large scale investment. There are limited online training courses available, which can increase awareness, this does not necessarily give professionals the expertise and confidence to deal with this complex condition in practice. This guideline places considerable responsibility on primary care to assess this condition, devise and review management plans and provide support for relapses which requires more than a one-off session.	the area develops. See evidence review B for the committee discussion on training. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula. *Development of training programmes* . Evidence reviews A and B include the committee discussion of the evidence and their experience that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS.

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BACME – British Association for CFS/ME professionals	Guideline	041	018	Our executive trustee patient representatives welcome the inclusion of carers in the draft guideline and emphasise both the patient and carer need to have confidence in the health professional (s) when discussing the illness, who should be open and transparent about the support available. Carers must feel listened to regarding the perspective they bring and the knowledge they have about the effect of the illness. Support and value family members in their new role and recognise their 24/7 contribution to the person with CFS/ME. Identify those who do not have the support of family and act quickly on signposting to possible support or setting this up. Access to a Community Matron, particularly for severe/very severe category, is invaluable. Our executive trustee patient representatives are concerned that the draft guideline does not acknowledge the carers' needs as they adjust to new roles; many give up employment to provide 24/7 care. Often carers report they feel undervalued for the work they do and are without wider family support. Their isolation and need for signposting and emergency support particularly for those more severely affected is not recognised in the draft guideline. Our executive trustee patient representatives recognise that the reality is some family members, including partners, may not be able to cope with the seriousness of the illness and leave.	Thank you for your comment. The committee agree that supporting families and carers is very important and have referred to the NICE guideline on supporting adult carers several times in the recommendations. This guideline has more detailed information to support families and carers.
BACME – British Association for CFS/ME professionals	Guideline	042	004	Energy envelope definition could benefit from refinement. It currently states: "The amount of energy a person has to do all activities without triggering an increase in their symptoms." We think that it should say:	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.

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				"The amount of energy a person has to do limited activities without triggering a flare in their symptoms" and then reference the definition of a flare (or dip). The reason for this amendment is that many people experience symptoms all the time, and for many, activity can be associated with a transient increase in symptoms. This transient increase in symptoms during or soon after an activity should not be conflated with a post-exertional symptom exacerbation. While the support measures included in this section can be helpful in the short term, there is no information included about strategies that facilitate progress. It is our experience of working with children and young people with ME/CFS, that information given at the outset is pertinent and should include evidence-based information about possible recovery and about what supports progress. The Guideline would benefit from clearer information about prognosis, stratified by age group rather than describing ME/CFS simply as "incurable".	*Long term outlook* After considering the range of stakeholder comments on this bullet point in recommendation 1.6.4 it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' This is to reflect the experience of all people with ME/CFS. Recommendation 1.6.5 referring to children and young people has been edited and 'usually' has been removed.
BACME – British Association for CFS/ME professionals	Guideline	042	017	The draft guideline describes under fatigability 'wired but tired' fatigue, or restless fatigue and relates this to hypervigilance during sleep. As specialist we commonly see this phenomenon and associated Restless Legs syndrome is common. We are concerned this is not referenced in the draft guideline. The advice given is to develop physical and cognitive winding down skills, which should be noted is difficult to master without specialist assessment to identify triggers and teaching and assessing interventions such as mindfulness to 'go down the gears' being present with sensations, challenging reactions and finding personalised soothing options.	Thank you for your comment. The committee note that restless legs syndrome is more common in fibromyalgia than ME/CFS and the most action is referral to a back to the person's GP and then to a neurologist. To note after considering the stakeholder comments this bullet point has been edited to, 'restlessness or feeling 'wired but tired'' and 'hypervigilance during sleep' has been deleted.
BACME – British Association for CFS/ME professionals	Guideline	042	026	The patient representatives of BACME suggested that the word flare be replaced by the term dip. They felt that the term "flare" is more commonly used for inflammatory joint disease, and Fibromyalgia Syndrome and that it did not represent their experiences.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.

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BACME – British Association for CFS/ME professionals	Guideline	043	043	This currently states: "For many people, physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen." This wording suggests that there are people for whom physical activity does not have health benefits. Physical activity has benefits for all people, but any physically disabling health problem will limit engagement with physical activity. The POTENTIAL benefits are true for people with ME/CFS as well, so it needs to be engaged in at a sustainable level, which is why the Guideline section on physical maintenance is so important. Other sections of the guideline emphasise the importance of energy management and we think that this section would benefit from reiterating this important advice. Physical activity, like all other activity, needs to be developed carefully and gradually at a level that can be sustained and maintained. For example, the wording could be "Physical activity has a wide range of health benefits but in people with ME/CFS, too much physical activity will cause a dip or a relapse. The principles of energy management should be considered if someone with ME/CFS is engaging with physical activity."	Thank you for your comment. After considering the stakeholder comments, 'for many people' has been deleted.' The section of the guideline with the recommendations for physical activity includes that the principles of energy management should be considered if someone with ME/CFS is engaging with physical activity'. When writing a guideline there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
BACME – British Association for CFS/ME professionals	Guideline	046	002	In this section on key recommendations for research, the committee have only focused on the need for more research around outcome measures for trial purposes. BACME recognises that one of the most important ways to ensure patient safety and to ensure that NHS services are delivering effective therapy programmes, is for there to be a standardised approach to clinical outcome measures. BACME therefore request that this recommendation is expanded to include clinically relevant outcome measures to be used by NHS specialist CFS/ME services.	Thank you for your comment. Research recommendations can only be made where the evidence has been searched for within the guideline. Clinical assessment tools were not included in the scope of this guideline as a topic to consider, and therefore the committee are unable to make research recommendations on this topic.
BACME – British Association for CFS/ME professionals	Guideline	066	027	Diet Although the draft guideline alludes to dietary advice it states there is not enough evidence to offer any dietary strategy which is very concerning. The Evidence Reviews highlight that patient	Thank you for your comment and information. *Dietetic support*

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				would like nutritional support, we are very concerned to find this important aspect is offered very little support and very limited reference to specialist input. Our members stress that if 60% of the immune system is in the gut then nutritional needs require careful individual specific dietetic specialist assessment, rather than standardised advice with the 'Eatwell Plate'. Specialist advice is essential to be tailored specifically to fatigue and understand the restrictions, sensitivities and sensory hypersensitivities, of taste in addition to smell, listed in the draft guideline. Associated symptoms of nausea and gastrointestinal disturbance are commonly reported but the draft guideline is not specific enough; only referring to nausea management. We are concerned that the guideline does not acknowledge the significant numbers who report irritable bowel and associated gut problems. Our patient representatives warn that patients are overwhelmed by the practicalities and organisational demands of planning shopping and cooking. We are worried that this aspect of the condition will not be taken into account in social care assessments. There are limited references to the more severe presentation. These patients are at high risk of malnutrition and it may not be appropriate to recommend FODMAP diet. The limited availability of dietitians specialised in the condition is also not addressed and the limited size of many specialist services makes managing dietetic assessments problematic. We are alarmed that the evidence reviews include alternative diet and supplement research which does not meet the research rigour many other studies are excluded on. Question 1: In order to assess fully with dietician's with insight into the condition there will be a big impact on practice. BACME	Despite the limited evidence on dietary strategies the committee thought it was important to make recommendations on dietary management and strategies. The guideline highlights the importance of diet and nutrition and support throughout the recommendations, it is part of the initial assessment and there is a comprehensive section in the management of symptoms section. This is also reflected in the section on people with severe and very severe ME/CFS. There are clear recommendations when people with ME/CFS should be referred to dieticians with a special interest in ME/CFS. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. To note the recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. To note no studies that met the protocol inclusion criteria were excluded from any of the evidence reviews.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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				support specialist referrals, however, specialist service provision is extremely limited. Question 2: As a result, there are significant cost implications Question 3: BACME could develop practical resources and nationally recognised examples of good specialist practice.	
BACME – British Association for CFS/ME professionals	Guideline	070	029	Question 3 re existing resources and examples of good practice: We are concerned at the claim that training programmes in ME/CFS are often out of date which will lower the confidence patients have in their providers. Specialist in the condition maintain their knowledge and application of current therapeutic skills through many routes. This point appears to be based on Committee speculation rather than reality. BACME's education programme, conferences, research newsletters, peer supervision and publications can provide the evidence to support fit for purpose education material. Many specialists provide training to other professionals including primary care staff, doctors in training and social care staff, all of which would be based on current practice. BACME are well placed to consult on the design and delivery of training and supervision through a national competency programme informed and endorsed by their members.	Thank you for your comment. This is reflected the evidence reviews A and B, expert testimony and the committee's experience that training materials are often out of date, however these reviews also reported that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS and this is the basis for recommending the development of training programmes by ME/CFS specialist teams.
BACME – British Association for CFS/ME professionals	Guideline	071	010 - 014	Question 1 re impact on NHS CFS/ME services and Question 2 re cost: There is a significant impact on NHS services of changing the name from CFS/ME to ME/CFS. For many services this will involve the service name having to be changed as well as changing all the materials the service use, which could be extensive. Services will have printed material for patients, referral forms for GPs, letterheads, information leaflets, online documents, group program presentations etc which will all require amendment. Much of the impact of making this change is likely to fall on NHS administrative staff who are already overstretched. For services who do not have administrative support, clinicians will have this task which will affect the time they have to see patients. There will be a cost implication linked	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental.*

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				with this change in terms of the cost of staff time and financial costs of rewriting printed and online material.	*For consistency, the abbreviation ME/CFS is used in this guideline.'* There is no requirement to immediately update signage and stationery. However, we expect that new services will use the guideline's nomenclature and that existing services will adopt it when it is time for them to reprint their materials.
British Dietetic Association	Evidence review H	498	K1.12	Comment This shows a range of ideas, and is a good start, other aspects of diet impact may arise from the research. As these dietary areas are listed here perhaps gut symptoms and the microbiota could be acknowledged in the nice guideline review as an area of interest for strategies. Without this it could be missed. NICE "Outcomes: Quality of Life, fatigue…" It is worth adding gastrointestinal symptoms here too, as an outcome measure as it does not really fall under the other headings.	Thank you for your comment. The evidence did not allow the detailed or specific of dietary strategies to be recommended and this is why the committee made this research recommendation. Gastrointestinal symptoms have been added to the outcomes.
British Dietetic Association	Evidence review H	498	K.1.11	Dietary strategies. Why this is important The use of dietary strategies in ME/CFS management is widespread. *NICE_ A randomised controlled study into the benefits of dietary strategies will add a meaningful contribution to the evidence base in the symptom management of ME/CFS. There is a need for high quality trials into the effectiveness and cost effectiveness of dietary strategies for the management of ME/CFS.* Comment This is good to see in the report, and paves the way for funding research into diet.	Thank you for your comment.
British Dietetic Association	Evidence review H	499	K1.12	Comment regarding study design and feasibility: The complexity and difficulty of undertaking diet research is often underestimated. Recruitment, compliance, logistical delivery of the project involving food. Drop out rates for severely affected, attendance for research in a poorly subject group, etc, these all add to the difficulty of the research, the funding needs and the project duration. This requires quite specific bioscience and clinical research teams expertise, and significant funding.	Thank you for your comment and information.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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British Dietetic Association	Evidence review H	499	K1.12	NICE "Other comments Importance Low" We are disappointed that this is thought to be of low importance. We feel this is important to ME/CFS sufferers and reflected in patient's self-modification of diet. Having more evidence in this area will enable us to shape future guidelines. Diet impacts on every system of the body, including immune system and microbiota etc.	Thank you for the comment. The importance here is relative to the research recommendations the committee prioritised. The committee acknowledged that any research in ME/CFS will be difficult until a diagnostic criterion has been agreed and populations for research can be uniformly recruited.
British Dietetic Association	Guideline	006	022	We welcome the mentioned of gastrointestinal difficulties or symptoms but this is not limited to those severely affected and GI symptoms are widespread features for less severely affected as well. Gastrointestinal difficulties are more commonly referred to as functional gut symptoms or IBS (Irritable bowel Syndrome) type symptoms or gastrointestinal symptoms.	Thank you for your comments. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline but would also clarify that symptoms in the section suspecting ME/CFS can be experienced by all people with ME/CFS. To note that gastrointestinal symptoms has been added to the symptoms that may be associated with ME/CFS in the section on suspecting ME/CFS and the IBS guideline added to the list of guidelines in the coexisting conditions section of the guideline.
British Dietetic Association	Guideline	009	013	1.2.4 - Inclusion in this section on the following symptoms may also be associated with, but are not exclusive to, ME/CFS: IBS (Irritable Bowel Syndrome) type symptoms / functional gut symptoms	Thank you for your comment. Gastrointestinal symptoms have been added to the list of symptoms.
British Dietetic Association	Guideline	009	013	1.2.4 - Sensory sensitivities include taste. Please add taste to section. This is mentioned in the draft later see comment 6 but needs adding here as well. In my experience this can present with specific new texture aversions additionally since the ME diagnosis. These can be very pronounced in the most severely affected impacting adversely nutritional intake and significantly limiting variety of foods eaten.	Thank you for your comment. Taste has been added to this bullet points.

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British Dietetic Association	Guideline	013	017 - 019	1.51 - bullet for diet assessment should include assessment of diet, food or gut related symptoms in order to pave the way for this to be included in management later.	Thank you for your comment. The list includes symptom management and links to the recommendations in this section including those on dietary strategies. As with all lists and examples they are not intended to be exhaustive.
British Dietetic Association	Guideline	031	002	1.11.28 1.11.33 to 1.11.39 - In Symptom management only nausea is mentioned. Other gut symptoms management not mentioned Dietary management and strategies 1.11.33 to 1.11.39 should include a numbered point to cover the dietary management of gastrointestinal symptoms, bloating, pain, wind, constipation or diarrhoea and signposting to the NICE guidelines (CG 61) on IBS	Thank you for your comment. The NICE guideline on Irritable bowel syndrome has been added to the guidelines listed in the coexisting conditions section of the guideline to signpost people with ME/CFS for support with these gastrointestinal symptoms.
British Dietetic Association	Guideline	033	009	1.11.41 - Add to poor appetite linked to altered taste, smell and texture tolerances. See comment 3	Thank you for your comment. This bullet point has been slightly reworded to include texture.
British Dietetic Association	Guideline	036	007	1.12.3 - Managing co-existing conditions. I am unsure why coeliac disease is mentioned in this context. Many with ME/CFS self-prescribe a gluten free (GF) diet which they believe helps the symptoms and many have gut symptoms. The draft does not acknowledge many with ME/CFS are following a GF diet and the need to check for Coeliac disease. Symptoms could be mistaken for Coeliac disease but in my experience ME/CFS rarely co-exists with coeliac disease. However here it would be appropriate to mention co-existing IBS symptoms and sign post to NICE guidelines on IBS (CG61)	Thank you for your comment. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not infer any importance of the condition in reference to co-existing with ME/CFS. After considering the stakeholder comments the committee removed the reference to the NICE guideline on Coeliac disease and added the NICE guideline on irritable bowel syndrome in adults.
CFS/ME Service for South Yorkshire and North Derbyshire – Children and	Guideline	General	General	The use of ME before CFS is a retrograde step suggesting that there is inflammation of the muscles and central nervous system. This is not the case. Changing this name will have significant impact on service's handouts, resources, signage, name badges etc and will be costly and time-consuming to change.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, 'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described

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Young People's Team					using many different names' and then readdressed in the context section of the guideline, 'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	General	General	We are concerned that this guideline will imply that CFS/ME is 'incurable' and the condition is 'hope-less', that people with the condition are passive in its prognosis rather than engaging in active strategies for recovery.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	008	012	4 weeks is not adequate time to consider CFS/ME in children and we suggest the 6 week timescale more realisitic. Discussing CFS/ME after 4 weeks may risk creating anxiety and reducing expectations of recovery.	Thank you for your comment. The period of a minimum of 4 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms at this point are given advice that may prevent them getting worse. In summary it would be unusual for an acute illness, including a viral illness to persist longer than this with all the symptoms. The committee emphasised it is the combination and interaction of the

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					symptoms that is critical in distinguishing ME/CFS from other conditions and illness. In addition to this the committee added additional recommendations at the 4 week point for children and young people ensuring that they are referred to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis. This the committee hopes will ensure that children and young people will have a correct diagnosis of ME/CFS. In addition the referral to community paediatricians for further investigations before ME/CFS specialist teams is the experience of committee members of working with children and young people. See Evidence review D- for the evidence and committee discussion.
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	014	019	We prefer the word 'setback' to relapse. Relapse suggests a passive illness-led process rather than one most likely triggered by biopsychosocial factors.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young	Guideline	024	004 - 005	"no current treatment". We are concerned that this stance ignores the effective work provided by specialist services who are able to make a considerable difference to many people with CFS/ME. Anecdotally our patients are distressed by reading this in on-line documents and books and requires careful discussion to reassure children and young people that improvement is possible.	*Thank you for your comment.* *Cure or treatment* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	027	008 - 009	This sentence 'do not offer any therapy based on physical activity' is extremely unhelpful and should be removed from the guidance. The document goes on to describe how physical therapy and energy management can be helpful if managed by experienced practitioners, presenting a confusing message. We are concerned this will have a negative impact on patient's expectations and undermine their willingness to engage in energy management.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Treatment or cure* To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to

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					avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS.
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	028	010	…'therapies derived from osteopathy…' etc This appears to be a direct and personal attack on Phil Parker and is out of place in this guideline. There may be other therapies that people with CFS/ME have tried, with good or bad results but these are not mentioned. We strongly ask for it to be removed on grounds of professionalism and impartiality.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee discussed the evidence for the Lightning Process and acknowledged that although some aspects of the therapy were found to be helpful, experiences varied. Some negative experiences were reported around the confusing nature of the educational component, the intensity of the sessions, and the secrecy surrounding the therapy. The committee were particularly concerned around the secrecy of the Lightning Process and the lack of public information on the components and implementation of the process. The committee discussed concerns that the Lightning Process encourages people to ignore their symptoms and push through them and this could potentially result in harm for people with ME/CFS. The committee noted they had made clear recommendations on the principles of

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					energy management and this is at odds with the principles of energy management in the guideline. In addition, the committee were aware that some children had been told not to discuss the therapy with their carer or parents. The committee agreed this was an inappropriate and harmful message to give to children and young people. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H). After considering the stakeholder comments the committee agreed to remove the reference to osteopathy recognising that the recommendation should be specific to the Lightning Process and not broadly osteopathy. We hope this clarifies that this decision is made on the evidence and is not a personal attack.
CFS/ME Service for South Yorkshire and North Derbyshire – Children and Young People's Team	Guideline	034	001	We are concerned that this recommendation does not acknowledge the range of psychological therapies that have potential to support people with CFS/ME alongside CBT, including ACT (Acceptance and Commitment Therapy), Compassion-Focused Therapy and Interpersonal Therapy. We suggest that this section should include a statement implying that therapies offered by psychologists and other trained professionals with experience of treating CFS/ME can be helpful.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
Chartered Society of Physiotherapy	Evidence Review G	General	General	Comment: The GETSET trial included only patients who met the NICE criteria for ME/CFS, and ALL patients reported post-exertional malaise (PEM) at randomisation. ALL the outcomes that were measured were shown to favour GET immediately after the intervention (fatigue, physical functioning, general symptom	Thank you for your comment. The GETSET study was not downgraded for indirectness as participants met the previous NICE criteria and all had PEM, however where results from this study were meta-analysed with other studies, the indirectness rating was judged based on the

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				scales, depression, anxiety, activity levels, work and social adjustment). Furthermore, guided graded exercise self-help was better at improving fatigue (and physical function to a lesser extent) than specialist medical care. There were no differences in the incidence of adverse events and no serious adverse reactions. This is with minimal guided GET support; it was safe AND helpful.	study or studies that contributed the majority of the evidence for the specific outcome, which may have resulted in the outcome being downgraded for indirectness. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. As part of this a subgroup analysis has been performed, which examines results from trials where ≥ 95% of participants had PEM separately (including the GETSET trial) to trials where <95% of study participants had PEM or this was unclear. See evidence review H appendices Fand G for full details on the approach taken, the analysis and the impact on the results and interpretation of the evidence. Clinical benefit or harms for each outcome are determined based on the minimally important difference (MID), not statistical significance or benefit/harms reported by study authors. Detailed information on this process can be found in the methods chapter.
Chartered Society of Physiotherapy	Evidence Review G	General	General	This guideline has reviewed the qualitative paper published from the GETSET trial (Cheshire et al. 2018 - https://doi.org/10.1080/09638288.2018.1499822). It presents a number of the findings from this paper, without giving the reader a full understanding of the full context and findings. Furthermore, some findings have been taken out of context. Comment:Firstly, the paper is based on 19 interviews with patients who volunteered to be interviewed from 107 in the trial. Secondly the trial was not supported GET as has been previously defined, but a guided graded exercise self-help (GES)	Thank you for your comment. There was no clear picture of benefit emerging from the quantitative evidence. The programme did not only appear to be challenging for some but there were important harms reported in the qualitative evidence for GET including the exacerbation of symptoms and worsening of comorbid conditions which the committee had to take into consideration when making recommendations. However, the recommendations were not solely based on the Cheshire et al study. The committee considered the benefits and harms associated with graded exercise therapy that had been

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				intervention. It is a self-management intervention that is patient-led but supported by a qualified therapist. The patients who took part in the trial and this qualitative study were on a waiting list for therapy in a specialist CFS/ME service. The positive qualitative patient reports of this approach (many of which have been overlooked in this draft guideline) may offer important insights around the importance of patient control when delivering interventions (Cheshire 2018 - https://doi.org/10.1080/09638288.2018.1499822). The aim of this study was to interview 9 patients who had been randomised to GES who reported being "much" or "very much" better, and 10 who reported being "much" or "very much" worse, compared to how they felt prior to GES. There were, however, zero patients who reported being much or very much worse, so the criteria was changed to include those who reported feeling "a little worse". The absence of any reporting being "much worse" in this group, and the overall outcome in the trial for this group being better than in the usual care group, should be reassuring that this minimal intervention is generally helpful for such patients. Furthermore, of the 10 who had rated their condition as "a little worse" compared to how they felt prior to GES on the 12-week follow-up questionnaire for the trial, four (40%) subsequently reported at the interview that they had felt "a little worse" due to other issues, and not GES. Two of these patients reported not really engaging with GES as a result of these other problems, but were intending to try it in the future, the other two reported they had in fact experienced a modest improvement with GES. The main finding that in both the "much better" and "a little worse" groups, some "found doing GES challenging, and personal motivation played a key role in participants sticking with their GES programmes." Interventions that aim to change	identified in the quantitative and qualitative evidence and their own experiences of these interventions The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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				people's lifestyle (as opposed to taking a pill) are often challenging for patients. This study illustrated this is also the case (unsurprisingly) in people with ME/CFS, and if the therapist is aware of these challenges in patients they can better support them. This should not be a reason to not recommend GET, but to look at how it can better delivered to support patients through the process, as well as which patients it is suitable for. An obvious outcome was that for those with longer illness and more severe symptoms, face to face sessions with a therapist and more sessions would have been more useful, and is what is offered in specialist clinics. That some experienced exacerbations in their symptoms following this GES programme should not be a reason to denounce GET, but to offer a more supported GET. This was only guided support self-management of GET, it was not face-to-face GET. Those in the "a little worse" group reported more co-morbidities suggesting that they needed more guidance and support from therapists. Suggestion: Please clarify this in the text.	
Chartered Society of Physiotherapy	Evidence Review G	General	General	Comment: A statement in the evidence review states: "Another finding of the guideline suggested that most found following the programme to be 'hard work'. The level of exercise was selected by the therapist and experienced by patients as too difficult." This statement is not a true reflection of the meaning of the statement in the paper (Cheshire et al. 2018 - https://doi.org/10.1080/09638288.2018.1499822). The study reported that participants (both those that improved with GES and those that didn't) reported GES as being 'hard work'. But this did not refer to the level of exercise selected by the therapist being too difficult – firstly these participants reported that they selected their exercise/activity levels and were only guided/supported by the therapists, who were described as	Thank you for your comment. Based on the wealth and variability of the information available, studies can contribute to more than one theme, often reflecting both positive and negative experiences. The information reported in all papers has been carefully extracted and reflects people's experience of the interventions they received, these have been organised into themes. Patient reports of the exercise intervention received being 'hard work' could not be discarded and together with information from other studies about the exercise intervention received being too

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				gentle, encouraging and understanding. Secondly, if participants found their activity too difficult, they reported being advised to reduce it to a previous level that they had found manageable. Rather it was sticking to an activity routine that was hard. People reported a number of reasons for this, including: 1) GES meant initially limiting the amount of activity that they could do (baseline is level of activity that an individual can do on a bad day) which was 'inconvenient', 2) progress could be slow, sticking to a set routine everyday may not be convenient and therefore temporary symptom exacerbations were experienced. To illustrate this point with an example, one participant said: "There was a point at which I was 'oh I'm just sick of this routine and I just want to do whatever I feel like doing'. So, actually the base-lining wasn't so frustrating as about a month in where I just felt like I need some bloody variation". Suggestion: Please clarify this in the text.	difficult, have been interpreted to contribute to the overarching theme named 'Too difficult'. However, taking into account the lack of depth in this data, as well as the possibility that 'hard work' may not necessarily reflect the same experience of difficulty emerging from other studies, this has been taken into account and have contributed to the low quality rating given to the theme. This is reflected in the description of the themes' assessment of confidence both in the evidence review's narrative summary of the review findings and in the qualitative evidence summary footnotes. In line with what you report, descriptions of therapists as gentle, encouraging and understanding have also been captured (as it can be seen in Evidence review H, Appendix D in the full extraction table for the Cheshire study) and have been synthesised together with findings from other studies to contribute to the overarching theme titled 'Therapist approach'. Furthermore, the example you provide about the need for variation has been captured as well and contributes to the overarching theme titled 'Overall approach'.
Chartered Society of Physiotherapy	Evidence Review G	333 - 334	011 onwards	Comment: It is not appropriate to summarise the findings of completely different studies under the heading 'Qualitative review of experiences of graded exercise therapy'. It is clear from just one study that there has been much misinterpretation and misrepresentation in this section alone. Some of the statements refer to the Cheshire 2018 paper (https://doi.org/10.1080/09638288.2018.1499822), but others must refer to other qualitative work as they are not relevant to the Cheshire 2018 work. However, it is unclear where each of these statements comes from and therefore for individuals to check their accuracy. One has to question how much of the interpretation of the findings from other qualitative research work has been misinterpreted and/or misrepresented through this guideline. Certainly, for this single study there have been	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: The manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. Findings emerging from different studies can be synthesised together under the same overarching theme. Based on the wealth and variability of the information available, studies can contribute to more than one theme, sometimes reflecting different experiences. We have thoroughly examined the information reported in all papers to extract all that reflect people's experience of the interventions they received and organise them into different themes to bring to the committee's attention. The

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				statements made that are simply not true, but only through reading the full paper would you know this. One example is that another key finding from the Cheshire et al (2018) study, but that is not really mentioned in the Evidence Review, is how valued and liked the therapists were, even by the participants in the deteriorated group. They were described and gentle and understanding and no participant reported feeling uncomfortable that they were misunderstood and being pushed beyond their limit. The importance of the training specialist therapists and the importance of the approach of therapists delivering the programme is important and as previously mentioned, unlikely to have been GET. Suggestion: Provide clarity and referencing so that it is possible to identify what statements have been attributed to particular research studies. Please verify that all reported findings are appropriately checked prior to inclusion, as inconsistencies between the research study and the reporting in this guideline have been identified.	extent to which different experiences emerging from the same study or across different studies contributing to a particular theme is also captured in the evidence synthesis and where qualitative experiences have differed, this has been captured through summarising different views under different themes (where there was information to support a separate review finding) or in the element of 'coherence' contributing to the overall confidence in each review finding (where there were also qualitative accounts that appeared to differed to the information conveyed in the review finding). The specific studies contributing to each review theme are specified in the footnotes of the GRADE tables in the 'Qualitative evidence summary' sections in both Evidence reviews G and H as well as in the 'Qualitative evidence synthesis' section in Evidence review G (2.1.5). In line with what you report, descriptions of therapists as gentle, encouraging and understanding have also been captured (as it can be seen in Evidence review H, Appendix D in the full qualitative evidence table for the Cheshire study) and have been synthesised together with findings from other studies to contribute to the overarching theme titled 'Therapist approach'.
Chartered Society of Physiotherapy	Evidence Review G	200	020	Comment: We note that two of the 13 included studies in your review of effectiveness (3 and 67) are unpublished studies. These have therefore not been exposed to peer review and issues surrounding quality, sampling strategy, conflict of interest, and therefore the applicability of findings need to be addressed. For example, the Forward ME survey 2019 was a survey set out to gather "evidence relating to long-term outcomes and harms following Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET)". The aim and survey questions are open to bias as they did not provide an opportunity for participants to comment on any positive experiences. This survey appears to have been sent to a selective group of people belonging to ME charities who may oppose the use of GET or CBT. NICE need to use similar rigor when evaluating all research	Thank you for your comment. In recognition that the views of people with ME/CFS who had experienced the interventions was important, the qualitative review was done with an accompanying call for evidence which allowed registered stakeholders to submit information relating to the review question. Evidence submitted within this call for evidence was assessed for inclusion in the evidence review in addition to the evidence identified in the systematic searches following the same process of assessment against the review protocol. The Forward ME Survey 2019 was included as part of the call for evidence. We agree there are important limitations that have been considered. The Forward ME survey 2019 has been downgraded for concerns over methodological limitations due to concerns over the recruitment strategy uses, the data collection method (including open ended questions focusing on negative aspects of treatment) and

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				considered including qualitative studies. Is there evidence that the patients responding to this survey had a verified diagnosis of ME/CFS or had participated in a graded exercise program with a specialised therapist? In our opinion, the figure reported of 67% of patients feeling worse after having GET does not reflect feedback from studies or clinics, where existing specialist ME/CFS clinical services report good feedback from patients and families, have long waiting lists and have to limit the number of sessions due to limited resources. The Forward ME survey has the highest level of risk of research bias and yet seems to have high importance in the outcome of this guideline. Other surveys and committee experience have been used to develop this guideline even though there is a high risk of bias associated with this. We have concerns regarding the high risk of bias from any findings from these studies due to their sampling strategy, whether GET has been appropriately defined, whether the participants actually received GET (and therefore whether respondents are reporting on their exposure to GET or GEA), especially as this has been misclassified in this guideline). Suggestion: This should all be explicitly be reported in the summary Table 69 and the guidance should be re-examined in light of these serious flaws. 65 Oxford Clinical Allied Technology and Trials Services Unit. Forward-ME Group CBT & GET Survey. 2019. 67. Unpublished study - Physios for M.E. An exploratory study of the experiences of M.E patients and physiotherapy	concerns over data analysis as explicitly specified in the qualitative evidence table for the survey in Appendix D on Evidence review H. This has been accounted in the assessment of confidence of review findings that the survey contributes to. The limitations in the evidence have been brought to the committee's attention and taken into account in decision making. In addition to this, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See evidence review H Appendix on PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed that in order for this criterion to be adequately met, self-reporting of PEM would not be sufficient and 95% of participants need to have been diagnosed by a health professional as having PEM. The Forward ME 2019 survey did not meet this criterion as 98.5% self-reported their experience of PEM. As a result, evidence from the survey was further downgraded for concerns over the applicability of the population. This is explicitly reported in the summary of included studies in evidence review G and in the Qualitative evidence table for this study (in Appendix D, Evidence review H) and reflected in the relevance rating component of the assessment of confidence in the findings emerging from the survey. This resulted in further downgrading the confidence in the relevant review finding from Moderate to Low quality. The same has been applied to the Physios for ME

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					survey also cited in your comment which has been further downgraded for concerns of relevance of the included population. The committee agreed methodological shortcomings are important and this approach has been followed throughout the guideline to ensure such shortcomings have been accounted in the assessment of confidence in the evidence/ evidence quality which contributes to decision making along with the variety of factors including the different types of evidence, the balance between benefits and harms, economic considerations, equality considerations and the committee's clinical expertise (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). No greater weight was placed on the findings of the Forward ME survey compared to other studies included in the evidence reviews and the evidence review was not the only source of information the committee considered when making recommendations; it was only part of the wide range of evidence that the committee considered, including that from, published peer review, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guideline, the committee also used clinical judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendations.
Chartered Society of Physiotherapy	Evidence Review G	333	019	Comment: Quoting from the Evidence Review: "Evidence showed that most people found stabilising their routine, choosing physical activity and setting their baseline level to be straightforward, but baseline levels were not experienced as sustainable and some experienced 'false starts' as they commenced the programme." To say that baseline levels were not experienced as sustainable by participants in this study is not true. All participants said finding their baseline (level of activity that they can do even on a	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts emerging from the Cheshire study have been synthesised and contribute to different review findings that the committee has considered, Negative experiences

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				bad day), was straight forward and they were able to do this. As participants begun increasing their activity - two participant experienced 'false starts', which in this study meant that they didn't properly engage with GES due to other things going on in their lives (e.g. one participant became homeless and was unable to start GES properly, another had pre-existing hip condition that needed treatment before she could start GES). Both these participants were about restart GET within a specialist service setting at time of interview, having resolved the separate issues that caused them to have "false starts". As the study reports: As participants commenced their GES activity (which involved completing an agreed additional physical activity), two participants in the "a little worse" (and none in the "much better") group described "false starts." That is, they reported not feeling physically/emotionally well enough to engage with GES. Suggestion: Please reflect these statements in the documents, and clarify how they are used to support the statements made by the committee.	including the statements you refer to also emerged from the study. These are equally considered by the committee regardless of how many people reported this as they also reflected the experience of some people. Please note that this was only part of the information that the committee has considered. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Chartered Society of Physiotherapy	Evidence Review G	333	022	Comment: Quoting the Evidence Review: "Most people noticed no immediate difference in symptoms, or an exacerbation during the initial phase which resulted in them not knowing if the programme was helping or hindering their condition and during this 'indeterminate phase', it was found to be difficult to maintain motivation." In all exercise programmes it takes time to notice improvements, they are not instantaneous, which is why they are 12 weeks. It has long been recognised known that symptomatic benefits of exercise programmes are seen irrespective of physiological changes (Pedersen & Saltin 2015 - https://doi-org.uea.idm.oclc.org/10.1111/sms.12581). This study illustrates that actually a minimal intervention may not be enough for some people with ME/CFS who would benefit from more support as they start a graded exercise or activity programme. It is not	Thank you for your comment. We are glad you think findings regarding motivation also reflect your awareness of what people tend to experience. Please note that this was only part of the information that the committee has considered. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are

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				unusual to struggle with motivation when undertaking an exercise programme, it is a well-researched phenomenon, and 'exercise psychology' is a discipline under the banner of Health Psychology for the scientific study of psychological factors that are associated with participation and performance in exercise and other types of physical activity. Motivation is one of the reasons why such a high percentage of the population remain sedentary despite knowing the benefits of exercise to their health.	developed). After the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional and this has been reflected in the recommendations made.
Chartered Society of Physiotherapy	Evidence Review G	334	038	Comment: "The committee noted the outcomes showing benefit were mainly measured at a relatively short follow up period of around 12 weeks." We acknowledge that long-term follow up data would be beneficial. Currently, the exercise/physical activity programming literature across many conditions would highlight that 12 weeks follow up is not unusual see (Geneen et al. 2017 see Table 3: https://doi.org/10.1002/14651858.CD011279.pub3) Suggestion: There should be a recommendation for further research to explore impact of holistic, person-centred physical activity programmes in people with ME/CFS, and studies to explore the suggested energy management strategies proposed in this guideline with long-term follow up. In addition, we ask that NICE request service data from ME/CFS clinics across the UK to gain longitudinal data.	Thank you for your comment. The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified this as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before recommending any research trials on physical activity or exercise interventions. The committee agree that the long term follow up of participants in trials is very important.
Chartered Society of Physiotherapy	General	General	General	References used in this response: • Candy B, Chalder T, Cleare AJ, et al. A randomised controlled trial of a psycho-educational intervention to aid recovery in infectious mononucleosis. Journal of Psychosomatic Research 2004;57(1):89-94. https://doi.org/10.1016/S0022-3999(03)00370-2 • Cheshire A, Ridge D, Clark LV & White PD (2018) Guided graded Exercise Self-help for chronic fatigue syndrome:	Thank you for these references.

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				patient experiences and perceptions, Disability and Rehabilitation, 42:3, 368-377, https://doi.org/10.1080/09638288.2018.1499822 • Clark LV & White PD (2005) The role of deconditioning and therapeutic exercise in chronic fatigue syndrome (CFS), Journal of Mental Health, 14:3, 237-252. https://doi.org/10.1080/09638230500136308 • Clark LV, Pesola F, Thomas JM, et al. Guided graded exercise self-help plus specialist medical care versus specialist medical care alone for chronic fatigue syndrome (GETSET): a pragmatic randomised controlled trial. The Lancet 2017;390(10092):363-73. http://do.org/10.1016/S0140-6736(16)32589-2 • Dougall D, Johnson A, Goldsmith K, Sharpe M, Angus B, Chalder T, White P (2014). Adverse events and deterioration reported by participants in the PACE trial of therapies for chronic fatigue syndrome. Journal Psychosomatic Research Jul 1;77(1):20-6. https://doi.org/10.1016/j.jpsychores.2014.04.002 • Gladwell PW,Pheby D, Rodriguez T & Poland F (2014) Use of an online survey to explore positive and negative outcomes of rehabilitation for people with CFS/ME, Disability and Rehabilitation, 36:5, 387-394, https://doi.org/10.3109/09638288.2013.797508 • Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011279. https://doi.org/10.1002/14651858.CD011279.pub3 Accessed 04 December 2020. • Kahlert D (2015). Maintenance of physical activity: Do we know what we are talking about? Preventive Medicine	

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				Reports. 2: 178-180. https://doi-org.uea.idm.oclc.org/10.1016/j.pmedr.2015.02.013 - King E, Beynon M, Chalder T, Sharpe M, White PD. Patterns of daytime physical activity in patients with chronic fatigue syndrome. Journal of Psychosomatic Research. 2020 May 23:110154. https://doi.org/10.1016/j.jpsychores.2020.110154 - Larun L, Brurberg KG, Odgaard-Jensen J, et al. Exercise therapy for chronic fatigue syndrome. Cochrane Database of Systematic Reviews 2019(10) doi: 10.1002/14651858.CD003200.pub8 - Nigg CR, Borrelli B, Maddock J, Dishman R. A theory of physical activity maintenance. Applied Psychology. 57(4): 544-560. https://doi.org/10.1111/j.1464-0597.2008.00343.x - Pedersen BK & Saltin B. (2015) Exercise as medicine – evidence for prescribing exercise as therapy in 26 different chronic diseases. Scandinavian Journal of Medicine & Science in sport. https://doi-org.uea.idm.oclc.org/10.1111/sms.12581. - Ried-Larsen M, Aarts HM, Joyner MJ (2017). Effects of strict prolonged bed rest on cardiorespiratory fitness: systematic review and meta-analysis. Journal of Applied Physiology Oct 1;123(4):790-9. https://doi.org/10.1152/japplphysiol.00415.2017 - White PD, Goldsmith KA, Johnson AL, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. The Lancet 2011;377(9768):823-36. doi: 10.1016/S0140-6736(11)60096-2 WHO guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. ISBN 978-92-4-001512-8 (electronic version)	

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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Chartered Society of Physiotherapy	Guideline	General	General	We recognise the need for the update to these guidelines and welcome some of the recommendations. However, we have a number of concerns which may impact on the quality of this guideline and its applicability in rehabilitation. These include 1) use of terms that are not consistent with clinical practice or research, 2) potential inconsistency in advice, 3) downgrading of prior research studies and Cochrane reviews, and 4) potential bias from selected qualitative evidence has not been fully taken into consideration.	
Chartered Society of Physiotherapy	Guideline	General	General	Comment: We feel using such a definitive statement as *do not offer people with ME/CFS any therapy based on physical activity or exercise as a treatment or cure for ME/CFS* is unhelpful and may result in the guidance being unable to be implemented. This is because terms such as exercise, physical activity, movement and physical maintenance are often used interchangeably across society and physiotherapy practice. The Committee's attempt to distinguish between terms is confusing and may lead to further misunderstanding for clinicians and patients. By focusing on specific terms, we feel that this guideline fails to recognise the nuances within rehabilitation strategies to improve function in all people with ME/CFS. One example where confusion may arise is in relation to the definitions of exercise and physical maintenance (see below). Arguably, one is describing the other, identifying that these terms are synonymous. "Exercise is planned, structured, repetitive and purposeful activity focused on improvement or maintenance of one of more components of physical fitness. Exercise is a subcategory of physical activity" (p.42 L.7). "Physical maintenance is the process of incorporating (planned, structured, purposeful) into daily (repetitive) activity a level of	Thank you for your comment. *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this. *Physical maintenance* After considering the stakeholder comments the physical maintenance section has been edited to add some clarity for readers. In summary the edits are: • The section has been renamed to physical functioning and mobility • text has been added to the recommendation to clarify this is about strategies to maintain and prevent the deterioration of physical functioning and mobility • text has been added that this should be small amounts and throughout the day • strength and endurance has been replaced by muscle function.

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				movement that does not exacerbate symptoms and ensures that joint and muscle flexibility does not deteriorate further than that caused by the condition so far. For many people with ME/CFS, this will be to ensure as much independence as possible in activities ranging from personal hygiene to daily living, working and social interactions (improvement or maintenance of one or more components of physical fitness). For the most severely affected, it may only be passive movements, which aim to maintain joint flexibility (components of physical fitness) and gently stretch muscle groups to avoid contractures developing. For some people with ME/CFS it can include physical activity which additionally assists bone health, posture and muscle strength (components of physical fitness). Such activity is undertaken within the person's energy envelope and avoids pushing through boundaries of tolerance." (p.44 L.7) The Committee does provide some clarification such as telling people about the risks and benefits of a physical activity programme (1.11.19). We wholeheartedly agree with this statement. However, this is contradictory to the main statement regarding exercise, and we feel there is a danger that these important messages around the potential benefits of physical activity will not be highlighted to people with ME/CFS. In addition, we feel the guidance does not acknowledge sufficiently the nuances of how the treatment of physical activity / exercise is applied clinically. This includes an appreciation that one's relationship with physical activity / exercise / movement / physical maintenance is not linear. It is a complex interaction of an individual's context and preferences together with biological, psychological and social factors, that change over time. Physiotherapists will work with people to identify value-based goals and it may be that for some people physical activity / exercise is absolutely at the core of their values and association with well-being and quality of life. Therefore, a goal including	*Physical activity and exercise* After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS.

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				physical activity / exercise is likely to form part of their management plan. Importantly, this will not be a 'one size fits all approach' but instead a patient-centred holistic approach, involving a biopsychosocial assessment and integration into the management plan. The application of this may involve additional skills including pacing, energy conservation and task rotation, as well as flexibility and compassion in relation to support progression and regression. We also strongly feel that a complete rejection of physical activity /exercise as part of the management plan for people with ME/CFS may cause significant adverse effects in relation to mental health. There is consistent evidence to show that people who are more active are less likely to develop depression (Schuch et al 2018) and anxiety (Schuch et al 2019) in the future. Additionally, sedentary time is associated with an increased risk of death compared to people who have a more active lifestyle (Ekelund et al 2020). Ekelund, U., Tarp, J., Fagerland, M.W., Johannessen, J.S., Hansen, B.H., Jefferis, B.J., Whincup, P.H., Diaz, K.M., Hooker, S., Howard, V.J. and Chernofsky, A., 2020. Joint associations of accelero-meter measured physical activity and sedentary time with all-cause mortality: a harmonised meta-analysis in more than 44 000 middle-aged and older individuals. British Journal of Sports Medicine, 54(24), pp.1499-1506. Schuch, F.B., Vancampfort, D., Firth, J., Rosenbaum, S., Ward, P.B., Silva, E.S., Hallgren, M., Ponce De Leon, A., Dunn, A.L., Deslandes, A.C. and Fleck, M.P., 2018. Physical activity and incident depression: a meta-analysis of prospective cohort studies. American Journal of Psychiatry, 175(7), pp.631-648. Schuch, F.B., Stubbs, B., Meyer, J., Heissel, A., Zech, P., Vancampfort, D., Rosenbaum, S., Deenik, J., Firth, J., Ward, P.B. and Carvalho, A.F., 2019. Physical activity protects from	*Management plan* The committee agree that a patient-centred holistic approach is important and this has been recommended throughout the guideline. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				incident anxiety: A meta-analysis of prospective cohort studies. Depression and anxiety, 36(9), pp.846-858. Suggestion: That messaging around physical activity supports that it may be beneficial to a number of people with ME/CFS, especially for those who value activity highly. We believe that the messaging within this guideline should support holistic, patient centred approaches to rehabilitation that support the integration of physical activity into patient management if: 1) it is what the patient wants, 2) it is highly monitored and supported by a specialist team, and 3) it is individualised and can be altered according to the symptoms of the person with ME/CFS.	
Chartered Society of Physiotherapy	Guideline	General	General	Comment: This guideline presents a very medical model, which seems retrogressive and diverging from current physiotherapy understanding and management of other overlapping and similar conditions such as chronic pain or fibromyalgia. The biopsychosocial model is widely accepted in the assessment and management of chronic conditions but is largely ignored in this guideline. We understand a lot of people with ME/CFS are frustrated with the lack of biomedical research and it is important that more biomedical research is funded to understand this complex disease. However ignoring psychosocial aspects, which will impact on any chronic condition, is not helpful. This is a very isolating condition and psychosocial factors can have a huge impact on quality of life and outcomes and should be included.	Thank you for your comment. The committee disagree the guideline presents a very medical model. A holistic personalised approach to the assessment and the management of ME/CFS is recommended throughout the guideline. The committee agreed to make some edits to the recommendations to the guideline and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Replacing 'comprehensive clinical history' in section 1.2' suspecting ME/CFS' and full 'history' in section 1.5 Assessment…by a ME/CFS specialist team' with medical assessment with physical and mental health included. • Recommendation 1.6.10 includes the importance of assessing and meeting the mental health needs of families and carers. • Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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					• the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders. As you note these are already included in the guideline under managing co-existing conditions.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: We find the use of the word "harm" throughout this document to be unclear and could be open to misinterpretation by the reader who may not understand the clinical meaning of 'harm'. Readers may assume that all physical activity is harmful, and therefore should be avoided, inadvertently exacerbating fear avoidance in those for whom supervised and structured physical activity may be beneficial. We feel strongly that experiencing a small and expected increase in some symptoms is not in itself harmful if approached compassionately and flexibly within an appropriately monitored, person-centred, personalised rehabilitation plan that is developed in collaboration with the person with ME/CFS. Suggestion: We suggest the use of alternative wordings such as negative impact / challenge (where appropriate) should be used to reduce the potential to induce fear in readers. If it is deemed that the use of the word 'harm' is crucial in this document, we request that the term 'harm' should be clearly defined in the glossary and explicit definitions for the degree of harm should be provided with relevant examples. This should provide context that some change in symptoms could occur following an assessment, increase in cognitive demands, stressful events, or change in activity and would also be labelled as harmful. This label should be applied consistently across the document if it is to be used, not just when describing physical activity. It should be made clear in the examples that any activity (cognitive, physical, emotional) has the potential to cause harm (i.e. an increase in symptoms).	Thank you for your comment. Harm is used nine times in the guideline and only in the rationale sections. Where it is used it is the context of an intervention being wrongly applied, increased burden and patient reported experience of harm and has been correctly applied.

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Chartered Society of Physiotherapy	Guideline	General	General	Comment: There is an assumption made in this draft guideline that proponents of graded exercise therapy consider that deconditioning is the cause of ME/CFS. We believe this point of view is misguided and not representative. However, deconditioning is associated with physical inactivity (Ried-Larson et al. 2017 - https://doi.org/10.1152/japplphysiol.00415.2017; WHO 2020 ISBN 978-92-4-001512-8), and deconditioning may perpetuate the symptoms of ME/CFS (Clark & White 2005 - https://doi.org/10.1080/09638230500136308). Therefore, maintaining activity levels at an appropriate level for each person with ME/CFS is crucial. Suggestion: This guideline should try to reduce opportunities for confusion. It should propose that a person centred, individualised approach should be used to support maintenance of or return to physical activity for people with ME/CFS.	Thank you for your comment. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation and replaced with 'perpetuating ME/CFS'. After considering the stakeholder comments the physical maintenance section has been edited to add some clarity for readers. In summary the edits are: • The section has been renamed to physical functioning and mobility • text has been added to the recommendation to clarify this is about strategies to maintain and prevent the deterioration of physical functioning and mobility • text has been added that this should be small amounts and throughout the day • strength and endurance has been replaced by muscle function. The committee agree that a patient-centred holistic approach is important and this has been recommended throughout the guideline. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) Physical functioning and mobility is included in the care and support plan based on the person's needs.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: The term "physical maintenance" is not a standard term or concept in rehabilitation or in ME/CFS. There is some research on use of 'maintenance of physical activity', which shows that it is not a term that has been operationalised (Kahlert 2015 - https://doi-org.uea.idm.oclc.org/10.1016/j.pmedr.2015.02.013), but we could	Thank you for your comment. After considering the stakeholder comments this section has been edited to add some clarity for readers. In summary the edits are: • The section has been renamed to physical functioning and mobility

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				find nothing on "physical maintenance" as a concept in this context. It is not clear in the section on 'physical maintenance' (on page 44) what it actually means in practice and how it could be undertaken, as it appears contradictory. The guideline recommends that people 'maintain' their joint mobility, muscle flexibility, strength and endurance. If they have been unwell for some time and have low levels or these, it will be difficult for them to work on this within the 'envelope', particularly in relation to cardiovascular health, bone health and muscle strength/endurance. In reality, a patient will need to gently extend their joint ranges and strength to gain benefit. It is just not possible to follow the current guidance and have 'physical maintenance' that will be helpful to all those parameters. However, thinking about support for maintenance of physical activity after a specialist-led graded exercise or physical activity programme is important (WHO 2020 - ISBN 978-92-4-001512-8), and requires more research (Nigg et al. 2008 - DOI: 10.1111/j.1464-0597.2008.00343.x), specifically in ME/CFS patients.	• text has been added to the recommendation to clarify this is about strategies to maintain and prevent the deterioration of physical functioning and mobility • text has been added that this should be small amounts and throughout the day • strength and endurance has been replaced by muscle function.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: It accepted that the Language used in healthcare can have a powerful impact on expectations and outcomes. The negative language used in this document (Do not, No treatment, No cure) is repeated numerous times and is unhelpful. The language used around physical activity is much more negative than that used around energy management, this risks increasing fear and perceived threat about physical activity and thus can have a negative impact on patients. We are concerned this guideline could worsen outcomes by increasing fear regarding the prognosis of CFS/ME and the impact of any physical activity programmes.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see

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				Suggestion: The order of wording such as risks or benefits in the document changes depending on the point being made and should be consistent to be balanced and unbiased Comment: These draft guidelines remove any sense of hope by stating that there is no cure or treatment. There are numerous specialist services across the UK that support people with ME/CFS to good clinical effect. In addition, there is evidence to support that structured incremental therapy programmes and cognitive behaviour therapy are of moderate benefit for people with ME / CFS. Clark et al. 2017 - http://doi.org/10.1016/S0140-6736(16)32589-2, Larun et al. 2019 – https://doi.org/10.1002/14651858.CD003200.pub8	recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. See evidence reviews F and G Non-pharmacological management for further information on physical activity and exercise. The GETSET trial is included in the review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: As there is no positive recommendation for exercise, how do we help the many patients who attend specialist services specifically with exercise and physical activity goals? These may include improving ability to undertake activities of daily living (ADLs) Suggestion: Please address these questions	Thank you for your comment. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					• the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. See evidence reviews F and G Non-pharmacological management for further information on physical activity and exercise.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: There are a number of references to the term 'cure' throughout the text. This term should be used carefully, and was to our knowledge purposefully not used in the 2007 guidelines. Suggestion: We suggest the term 'Recovery' be used in its place.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Chartered Society of Physiotherapy	Guideline	General	General	Comment: The direct links to the committee rationales are very helpful in the structure of the guidance- could direct links also be added to the public and patient relevant section resource?	Thank you for your comment. The links to the 'information for the public' are not added into the rationale as the guideline webpage includes a tab to the information for the public.

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				Suggestion: Please provide links between corresponding sections in the main document and the lay language version	
Chartered Society of Physiotherapy	Guideline	008 - 010	001 010	Comment: There does not seem to be enough information here on how clinicians can assess and diagnose patients suspected of having ME/CFS. The previous guideline was much more comprehensive here, suggesting, for example, which blood tests might be useful. Furthermore, whilst we agree it is important to offer support and early advice on management for people suspected of having ME/CFS, we would suggest that in usual clinical practice, that a formal diagnosis should not be made until all other potential diagnoses have been considered and excluded (as described in the 2007 guidelines). Suggestion: Provide recommendations for investigations to support the diagnosis of ME/CFS	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'.
Chartered Society of Physiotherapy	Guideline	028 - 029	023 - 002	Suggestion: The following should be included to detail the 'Ideal Physical Activity Programme'. • In this summary we will use the following terms which are now well-recognised in this field: ○ Setting a baseline: A baseline is a specific measure of activity that can be undertaken regularly without causing a worsening of symptoms. ○ Pacing: Pacing describes a range of tools and techniques to regulate activity and to manage activity. These including breaking activity down into smaller amounts, planning, or prioritising. • This 'updated version' takes into account patient feedback and has clarified and enhanced the collaborative and flexible aspect to a programme, which seems to have been significantly misunderstood. We	Thank you for your comment and information. The committee note that the detailed information you give compliments much of the principles in the recommendations.

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				have also sought to make the distinction between 'general exercise advice' and physical activity programme, which is essential, and re-worded the section that gives some warnings about exercise. 1. Partnership and collaboration: a. When increasing physical activity, it is especially important to listen closely to patients, working flexibly with their life and health circumstances and agreeing first a baseline level of activity and subsequently incremental steps collaboratively. This will allow a programme to be individually tailored and adjusted according to individual feedback. b. At any time, a patient can stop or pause the programme. c. Any steps that are taken towards an increase in physical activity must align with the personal goals of the patient. 2. Key Principles when delivering a physical activity programme: a. Physical activity needs to be delivered at the right 'dose' of frequency, intensity and duration. When started at too high a baseline, progressed too quickly, or with increments that are too large, it is likely to be unsustainable and cause excessive symptom exacerbation and setbacks. b. Patients should not be given inflexible or prescriptive programmes; it is essential they are person-centred and tailored individually. c. Programmes need to be regularly monitored, with careful attention given to the patient's	

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				symptomatic response and other factors in their life before, together, deciding whether to increase, decrease or maintain physical activity. Some on the other hand, can keep the physical activity at a similar level but may benefit from being more consistent. d. At any point during the programme, for some patients it may be appropriate to encourage physical activity, whilst for others it may be useful to hold back a little to help regulate activity and significant post-exertional impact. e. Programmes are best delivered one-to-one where possible, either face-to-face or virtually, over a number of months. However, some aspects of the programme can be delivered in groups as long as patients are able to make individual decisions according to their own circumstances. 3. Getting the starting point right: a. We recommend that, prior to attempting to increase physical activity, the patient is managing with their current level of everyday general low-intensity activity and that they feel ready and able to take the next steps. b. In the first instance, it is important that there is a joint understanding of the everyday reality of a patient's life including physical. emotional and cognitive components. Activity diaries can be used to document and analyse daily physical activity routines. c. Non-incremental pacing techniques can be very helpful to stabilise daily routines and ease symptoms. They can form a valuable foundation from which to build upon.	

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				4. Assessment: a. We do not recommend extensive or intensive physical assessment beyond the assessment the patients have already had in coming to their ME/CFS diagnosis. b. Where physical assessment is appropriate, it should be brief and assess global or major loss movement or use simple measures to determine current functioning. 5. Goal setting and programme planning: a. A therapist and patient should jointly decide what specific physical activity is important in the patient's life, and seek to analyse the main physical components of this activity (eg endurance, flexibility, strength required). b. Once the components of the activity have been collaboratively understood, a plan can be developed that acknowledges the steps that could lead towards reaching such a goal from their current starting point. 6. How to know when to increase, decrease or maintain activity: a. The physical activity programme should be flexible to the individual, and adjusted according to: i. Patient preference and choice ii. Current symptoms and their severity and impact on daily life iii. Whether symptoms are improving, the same, or getting worse	

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				iv. Current or likely future changes in the level of activity (eg an upcoming event, holiday etc). v. Active infection (eg fever, chest infection). vi. General response to the previous planned physical increment b. Physical activity should be decreased if the patient has an active infection, a significant symptom exacerbation or setback, or if they are finding physical activities too difficult. They should also be reduced if a physical activity level is unrealistic and cannot be maintained. If this is the case, a baseline of sustainable activity should be agreed, with encouragement to build back up again to previous activity levels as able. c. Physical activity should be maintained if the patient feels able to do so, whilst also keeping in balance with other important aspects of their lives. Once they can maintain physical activity sustainably, the programme should be reviewed to see whether an increase may be appropriate at that time. d. Physical activity can be increased: i. When the patient agrees to explore progressing further ii. When the patient feels able to take a small incremental step and this can be planned into their routine iii. When the general level of everyday activity is relatively stable iv. When they are feeling better after the previous increase in activity. NB: It is normal to expect a temporary but	

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				manageable increase in symptoms as a patient goes from one increment to the next, and for this to settle down if the activity is undertaken routinely. Subjective measures such as a perception of effort scale can be used to help monitor the experience and to help indicate the right time to increase again. 7. How to increase activity a. Clearly determine a specific measure of physical activity that can be completed regularly without increasing symptoms. This should be a level that the patient feels confident that they can do on at least 5 days in each week. Therapists can assist patients in determining this baseline level, and to help set a realistic goal, which may sometimes be less than they are currently doing or would like to do. The aim in this first stage is sustainable activity, undertaken regularly. b. This may be sitting up in bed or brushing hair, for example, for people with severe CFS/ME, or gentle stretches or a slow walk for those who are more mobile. c. Once this level can be achieved sustainably and regularly, the therapist and patient can jointly decide whether an incremental step can be taken. d. At first, the increases in physical activity tend to be increases in duration (rather than intensity), keeping the frequency at 5 days per week. Increases in duration tend to be comfortable for patients at around 10-20% but	

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				the exact degree of increase should be jointly negotiated. This might mean, for example, 5 minutes to 6 minutes walking, or someone more severely affected might sit up for longer. e. Patients are encouraged to see any mild increase in symptoms that correspond directly to an increase in activity as normal, and reassured that this is likely to reduce as they continue at this new level. If significant or distressing symptoms occur, it is appropriate to reduce the physical activity to find a new sustainable level, or baseline. f. The programme can continue to increase in duration, following b. and c. as above, until a patient can either achieve their goal or until 20-30mins of duration is achieved. g. Once 20-30 minutes of regular physical activity (approximately 5 days per week) can be achieved, the intensity of the activity can be increased. If the patient's goal is towards exercise (eg gym or dance class, cycling etc), the intensity can be carefully controlled by monitoring heart rate for those who would find this helpful. If the goals are not towards aerobic exercise, then the programme at this point might focus on increasing endurance or strength. 8. Other aspects to consider: a. Managing and increasing other activity (including functional, cognitive, vocational, social, family) can be managed using similar principles.	

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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Chartered Society of Physiotherapy	Guideline	027 - 028	021 029 (p028)	Comment: There are a number of statements made about what NOT to offer people with CFS/ME. Most of these relate to the use of exercise and/or physical activity as a treatment. A number of points to make on this: 1) These recommendations contradict every statement made in the guideline about 'referral to specialist services' as these will be providing a rehabilitative/incremental approach, which is based on the scientific evidence. 2) It assumes that GET recommends 'fixed incremental increases', which is inaccurate (White et al. 2011 - doi: 10.1016/S0140-6736(11)60096-2; Clark et al. 2017 - http://do.org/10.1016/S0140-6736(16)32589-2). 3) It assumes that GET is based purely on 'deconditioning as the cause of ME/CFS' which is also inaccurate (White et al. 2011 - doi: 10.1016/S0140-6736(11)60096-2; Clark et al. 2017 - http://do.org/10.1016/S0140-6736(16)32589-2). 4) It confuses GET with physical activity programmes (PAP) and generalised exercise advice (GEA). We feel these draft guidelines have confused 'Graded Exercise Therapy' (GET) with what we might call 'general exercise advice.' (GEA). As made clear in the NICE 2007 guidelines, these are two very different concepts, with very different results. These draft guidelines specifically state to NOT USE Graded Exercise Therapy. However, the recommendations suggest supported, incremental increases in physical activity and, starting from an established baseline which are hallmarks of GET. It appears that these guidelines should suggest that people do not use generalised exercise advice (GEA), but that approaches that have similar principles to GET should be used. This confusion needs to be urgently rectified.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for physical activity including graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This, when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects

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				Suggestion: We suggest that the following advice for the development of 'recommended' and 'not recommended' approaches to physical activity be used: b. We agree with NICE and with patient groups that we do not recommend 'general exercise / physical activity advice'. This is any programme that is unsupervised, unmonitored, inflexible exercise advice delivered by untrained generalists. This is what we would call 'general exercise / physical activity advice' which could be anything from a therapist delivering a general exercise programme, to a GP recommending that the patient 'exercise more', 'be more active', 'do Couch to 5K', or an inflexible programme delivered over only a few sessions. GEA, given its uncontrolled nature, does have the potential to cause problems for patients, particularly if delivered in an inflexible non-collaborative way that is too hard, progressed too quickly, or if the advice encourages increments that appear prescriptive or too large. When patients talk of 'harms', we strongly believe (if the advice received was fully explored, or if the patient surveys were strict about their definitions) they would be referring mainly to GEA (Gladwell et al. 2014 - https://doi.org/10.3109/09638288.2013.797508). c. The programme that we do recommend is a collaborative, supervised, monitored, individualised *and flexible* programme delivered by trained specialists. It is delivered	the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation and replaced with 'perpetuating ME/CFS'. Based on the evidence mentioned above and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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				one-to-one, according to the individual goals of the patient, and the programme extends to 15 sessions. The physical activity programme is characterised by very well controlled, gradual, increments introduced flexibly when a patient is ready. Increments may also be stabilised or reduced as appropriate. d. There are fundamentally important differences between 'general exercise advice' and a person centred, individualised, planned and monitored physical activity programme delivered by a trained specialist. It is essential that therapists and patients do not confuse the two.	
Chartered Society of Physiotherapy	Guideline	001	009 onwards	Section: "Who is it for". Comment: It is our opinion that there is not sufficient information in this guideline to support the listed professionals to deliver an intervention. We have concerns that the guidance in regarding physical activity is contradictory and there is a lack of helpful occupational / return to work guidance. We request that these be addressed in future drafts.	Thank you for comment. *Delivering interventions* After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed).

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					This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Supporting people with ME/CFS in work, education and training* After considering the stakeholder comments further information on types of adaptions and adjustments are included in the committee discussion in evidence review A.
Chartered Society of Physiotherapy	Guideline	005	006	Comment: "use a person-centred approach to assess people's need" Suggestion –change the wording to "a person's needs"	Thank you for your comment. After taking into consideration stakeholders comments this has been edited to 'use a person centered approach to care and assessment'.
Chartered Society of Physiotherapy	Guideline	006	007	Comment: The guideline only provides detail for awareness of people with 'severe or very severe'. This does not explain the problems that people with mild / moderate symptoms may be experiencing and may be alarming for individuals to read, if there is no explanation of the breadth of symptoms and their severity. Suggestion: Include a description of mild / moderate symptoms within this section. Add more examples / emphasis for people with mild/moderate ME and do not solely focus on those that are severely affected by ME/CFS.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section.

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					To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
Chartered Society of Physiotherapy	Guideline	010	001	Comment – Could the committee add examples into recommendation of what specialisms would be appropriate? In its current format, the recommendation does not support primary care clinicians with decision making. Also, there is no mention of specialist ME/CFS services. Suggestion: Please identify possible specialties that could support diagnosis. Mention of specialist services should be included earlier within this section. Suggestion: Consider additional wording such as 'For example, …. ' and provide examples or guidance on which 'appropriate' specialists to seek advice Suggestion for possible wording '…consider seeking advice from an appropriate specialist guided by the other most predominant symptoms- pain, joint or muscle symptoms, neurological symptoms, sleep disorder in addition to fatigue.	Thank you for your comment.
Chartered Society of Physiotherapy	Guideline	010	018	Comment: Use of the term "Energy envelope". We feel the term "Energy Envelope" is used liberally throughout this document without a clear definition provided in the glossary. This leaves the phrase open to misuse and misinterpretation. The term energy envelope is not a scientific concept or term, or one that is familiar to people outside of the ME/CFS field. We assume it is the same as the better known and scientifically tested 'adaptive pacing' approach, which is a non-incremental treatment, and as described later in the guideline, emphasises a 'reduction' in physical activity. The largest trial of this approach delivered outcomes that were either no better than *or worse than* a control group receiving only	Thank you for your comment After considering the stakeholder comments the committee agreed that the concept of an energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.

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				medical treatment (Dougall et al. 2014 - https://doi.org/10.1016/j.jpsychores.2014.04.002; White et al. 2011 - doi: 10.1016/S0140-6736(11)60096-2). We find it concerning that this guideline promotes a concept that may contribute to physical deterioration. Suggestion: Improve the definition of the term energy envelope in the glossary. Clearly define whether the 'energy envelope' is a fixed entity or whether it can change from day to day. Can clear advice on determining the 'energy envelope' be given if this is the core benchmark for managing the condition? We would also ask NICE to justify its support for a non-incremental approach, which is in opposition to the current evidence base.	*Adaptive pacing and energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. *Non- incremental approach* *With regard to physical activity and exercise, the committee concluded that fixed incremental increases are not recommended for people with ME/CFS.*
Chartered Society of Physiotherapy	Guideline	012	011 - 013	Comment: This recommendation is not fully consistent with recommendation 1.8.4. which includes virtual consultations within the recommendation.	Thank you for your comment. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms

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				Suggestion: Could the committee consider adding virtual assessment options, including video consultations and offer the choice of home visits or video consultations?	experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
Chartered Society of Physiotherapy	Guideline	012 022	021 017	Comment: We welcome the integration of self-management techniques into the management of people with ME/CFS and the recommendation for future research in this field. However, we find the terminology used in this guidance does not match the current scientific literature, and so does not appear to be evidence based. The term 'energy management' is a new term in ME/CFS and recommends that all people with ME/CFS stay within their energy envelope. This approach is not supported by scientific literature. We support the recommendation for patient centred approaches to care and for self-management. However, in our clinical experiences, many patients with ME/CFS seek support after experiencing boom-bust cycles and many find it difficult to self-manage without support.	Thank you for your comment Energy management is defined in the terms used in the guideline. See Evidence reviews G and H for the evidence and committee discussion on self- management strategies and energy management. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.

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				Suggestion: If these new terms are to be adopted widely, please provide clear definitions and a rationale for these terms, i.e. what is the evidence that underpins how they are to be applied?	
Chartered Society of Physiotherapy	Guideline	014	022 - 024	Comment This wording as it currently is structured may be realistic but also pessimistic – starting with 'Although…could it be reworded to provide a 'positive direction' for the future as per the committee evidence link that people can recover or go into long term remission.. There does not appear to be sufficient evidence that effective management is not achieved in many people. Can the possibility of reducing impacts through effective self-management be included? The current recommendation wording does not adhere or reflect the people's preference for the guidance in Main Findings P 18 'Need for a positive diagnosis & future direction15, 58, 87: Patients reflected on the importance of a positive direction for the future and on the need for the ME/CFS diagnosis to be framed in a positive way to enable them to maintain hope for improvement. ' Suggested rewording 'varies in long-term outlook from person to person - some people recover or have a long period of remission and other people will need to adapt to living with ME/CFS	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet points and hope this addresses your points: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
Chartered Society of Physiotherapy	Guideline	014 027	001 020	Comment: Children and young people tend to have a better prognosis and often improve significantly. The guideline does not make this clear and has very little guidance for younger people. It offers little advice regarding return to education or how to return to enjoyable or functional activity. Young people who have ME/CFS may wish to be able to return to education, enjoyed activities with friends and family, functional activity and even	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have

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				formal exercise and sports and PE. There is no mention of how to do this safely. Without increasing their baselines young people may not be able to return meaningful activities or reach their goals. Schools are often large buildings and being able to walk between lessons, or from the bus stop or manage stairs is of great value. Young people may say they don't want to be different from their peers and decline walking aids. By increasing their exercise tolerance / baseline this can make school more manageable and reduce setbacks that can result from participating in activities beyond their baseline. It is vitally important to provide some hope, not false hope but hope that is realistic based on experience with other young people. Some young people with ME /CFS also have orthostatic intolerance and hypermobility both conditions can be exacerbated by inactivity and deconditioning and can benefit from specific graded flexible activity programmes or modified programmes specific to those conditions. Suggestion: Please provide further detail on the management of children with ME / CFS.	as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Chartered Society of Physiotherapy	Guideline	024	002	Comment: The first statement in the section about 'Managing ME/CFS' refers the reader to "relevant NICE guidance for managing symptoms associated with ME/CFS that are not covered in this section" needs relevant references added to it and signposting within the document. Suggestion: Please add links to the relevant guidelines for managing symptoms with ME/CFS. This section would benefit from being more comprehensive in terms of the guidelines referenced.	Thank you for your comment. This link has been deleted here and added under symptom management for ME/CFS. In the co-existing conditions section of the guideline the links to relevant NICE guidance are added there.

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Chartered Society of Physiotherapy	Guideline	024	004	Comment: Graded exercise therapy (GET) and CBT (Cognitive Behavioural Therapy) have been shown to be safe and moderately effective treatments. This draft guideline removes these two rehabilitation approaches by downgrading studies that did not mandate symptoms of post-exertional symptom exacerbation as a symptom within their diagnostic criteria. This has excluded almost all the trials for these treatments which used the the CDC and Oxford criteria for CFS. These criteria are the most uniformly applied criteria in many research studies, especially those that are older. Suggestions: Clearer justification for the exclusion of studies that use the CDC or Oxford criteria is required.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Exclusion of studies No studies that met the inclusion criteria for the review protocols were excluded as you note the evidence was downgraded on indirectness of the population.
Chartered Society of Physiotherapy	Guideline	024	021	Comment: We agree that there the approach to physical activity for people with ME/CFS should be a flexible, tailored approach so that activity is never automatically increased. However, the recommendation to "progress during periods when symptoms are *improved* and allow for the need to pull back when symptoms are *worse*" is counter to the scientific research findings. If patients do more on a good day, they may then develop post-exertional symptom exacerbation, and so this advice may encourage a boom/bust cycle. Suggestion: Reconsider the phrasing of this sentence. This needs to reflect collaborative and patient centred approaches to management which can support increases in physical activity when the patient is ready, and after ensuring that their symptoms have been stabilised for a sufficient period.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse)'.
Chartered Society of Physiotherapy	Guideline	025	015	Comment: The section on 'energy management' appears to be describing the first part of a GET programme, when patients are setting a baseline. And, for some patients who are either in a boom/bust cycle of activity or general overactivity (King et al. 2020 - https://doi.org/10.1016/j.jpsychores.2020.110154) this will require a reduction in their activity at first.	Thank you for your comment. This committee agree that energy management support should use a flexible tailored approach and throughout the guideline the committee reinforce the importance of a personalised approach to care and support.

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				More information is required in this section about how patients and those supporting them can monitor physical activity. All of this is available in the 2007 guidance under 'activity management' and should be provided. Some patients will need to do less, some will not be able to do less, some will not need to do less, and most importantly this recommendation needs to be individualised and 'flexible'. The only way to know if people need to do less, stay the same or just change the pattern of their day is by asking them to complete an activity diary. In this guideline, the meaning of low, medium and high activity levels is not clear, more information would be required to support patients, clinicians and specialists. Suggestion: Provide greater detail in this section. Please identify 1) how activity levels should be monitored, and 2) how and when these should be reduced /altered (and how to identify when to do so).	There was a lack of effectiveness evidence on tools to support recommending people to monitor activity management. However, the committee considered the qualitative evidence (Evidence review G-Non pharmacological management) and their experience about the benefits of people using tools to monitor activity alongside the potential harms of increasing their burden and causing anxiety about activity levels. On balance the committee agreed it was important that self-monitoring of activity was acknowledged and where used it should be as easy as possible.
Chartered Society of Physiotherapy	Guideline	026	001	Refer people to a specialist physiotherapy or occupational therapy service if they: have had reduced physical activity or mobility levels for a long time' Comment 1: This recommendation is vague. Suggestion 1: Please qualify what is meant by a long time. Comment 2: Since there are so few specialist ME/CFS clinician Physiotherapists and Occupational Therapists and long waiting times to be seen - Could the committee offer stronger guidance on what interim intervention is to be given to support people waiting to be seen in specialist services? Delayed care waiting for specialist input that cannot be accessed may be as harmful as care by a non-specialist clinician as a result of the recommendation that intervention should only be performed by a	Thank you for your comment. Comment 1. 'for a long time' has been removed and a link to has been added to this section. Comment 2. The guideline includes a section on advice for people with suspected ME/CFS while they are waiting for a diagnosis and to be seen by ME/CFS specialist service.

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				specialist clinician- has the committee considered any potential harm- e.g. physical or mental health? Suggestion 2: Please offer stronger guidance on what interim intervention is to be given to support people waiting to be seen in specialist services?	
Chartered Society of Physiotherapy	Guideline	026	017	Comment: We welcome the statement to include physical maintenance in the management plan for people with ME/CFS. However, these bullet points are contradictory to advice given in 1.11.16 and creates ambiguity. The bullet points listed below (joint mobility, muscle flexibility, postural and positional support, muscle strength and endurance, bone health and cardiovascular) list features of exercise and fitness (which are supported in recommendations 1.11.18 and 1.11.19. Suggestion: Please clarify. It is our opinion that individualised, person centred physical activity programmes that are highly monitored and negotiated with the person with ME/CFS should be provided, if desired by the person with ME/CFS.	Thank you for your comment. After considering the stakeholder comments, 'Include strategies to maintain and prevent deterioration of physical functioning and mobility in the care and support plans for people with ME/CFS. Strategies may need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the care and support plan and the priorities and symptoms that people may have. In addition, the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Chartered Society of Physiotherapy	Guideline	027	021 - 023	Comment: We would absolutely agree with the recommendation that unstructured or inflexible exercise should not be recommended, and this was already stated in the 2007 guideline. However, using terms such as physical activity programme (PAP) generally without defining their meaning, could simply open up the possibility that more therapists will deliver 'general exercise advice' Suggestion: Please provide a clear description of what a PAP is and how it is delivered, so that specialists engaging in the rehabilitation of people with ME/CFS can ensure they are providing interventions in line with this guidance.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The recommendations at end of the physical activity and exercise section to provide further detail on the principles of a programme noting this is a personalised physical activity or

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					exercise programme that is overseen by a physiotherapist in a ME/CFS specialist team. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Chartered Society of Physiotherapy	Guideline	027	024	Comment: 'Do not offer' is a strong recommendation for physical activity. We assume there is strong evidence to support this statement. In addition, this contradicts recommendation 1.11.8 and 1.11.19. There must be evidence to support these two recommendations and therefore this statement needs to be tempered. Suggestion: Remove the 'Do not offer' statement. There is insufficient high quality evidence to support this statement, and it is directly contradicted by two recommendations within this guideline. Could something be added to link this with the energy envelope – not beyond the person's energy envelope Please clearly state that physical activity should be provided by appropriately trained specialist clinicians when appropriate. This should be made very clearly is the general perception of this guideline is that all activity is harmful and people with ME/CFS should not participate in physical activity.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the

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					review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Chartered Society of Physiotherapy	Guideline	028	006 - 007	Comment: This is factually incorrect. Graded exercise therapy (GET) is an evidence-based treatment for this condition, is supervised and monitored by a trained therapist in this condition, is not rigid, fixed or inflexible (it is mutually agreed and negotiated with the patient) and involves stabilising activity before embarking on an appropriate graded programme. Unfortunately, misunderstandings about the difference between GEA and GET is widespread. Some patients believe they have had a GET programme whereas in fact they have had GEA. A problem also exists that some untrained therapists who lack understanding of ME/CFS mistakenly provide GEA, when they believe they are providing GET. The most important failure in definitions in this document is where the draft guideline specifically recommends, "not to undertake an exercise programme with inflexible increments, like Graded Exercise Therapy." Increments in GET are entirely flexible, so this is referring to 'inflexible exercise advice', which is not part of GET. We agree NICE should not recommend GEA. However, therapists will need to know what to provide. By stating do not offer GET, and removing the clear descriptions of therapy given in the 2007 guideline, NICE removes one of the only effective tools therapists have to support patients. Suggestion: That graded exercise therapy is removed from this statement, and all additional references to GET as providing fixed incremental increases be removed. NICE should consider	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise

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				describing what a physical activity programme should consist of, as was previously provided in the 2007 guideline.	therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Chartered Society of Physiotherapy	Guideline	028	006	Comment: The statement *do not offer GET* contradicts the 2007 guideline despite more research having been published since to support its use (e.g. Clark et al. 2017 - http://do.org/10.1016/S0140-6736(16)32589-2), and a Cochrane Review (Larun et al. 2019 – http://doi.org10.1002/14651858.CD003200.pub8). These studies show that in clinical trials, supervised approaches to implement incremental approaches to physical therapy are safe. Whilst we acknowledge that some of the qualitative evidence reports poor experiences with GET, there are serious issues with the quality of conclusions that can be drawn from these studies. Firstly, in	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about

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				most instances, it is not known whether they were provided with GET (as provided in the research studies) or an unstructured exercise programme, sampling issues introduce bias in that it cannot be determined that these samples are representative of the ME/CFS population, potential conflicts of interest have not been declared. We feel the strength of the evidence used to generate this statement is not of sufficient rigour, and further rigorous research is needed using mixed methods approaches. The strongest evidence we have concludes that incremental approaches, such as GET, are the most effective therapies we have to date for ME/CFS. The GET incremental approach has been distilled, clarified and manualised so it can be delivered and researched in the form of Graded Exercise Therapy (GET). However, in practice, specialists use a range of tools and may use different names for what they do, but what unites them is the concept of incremental therapy – i.e. collaboratively planning gradual increases in activity when the patient is ready and able to progress. Due to the inappropriate over-emphasis of the non-incremental approach, and specific downgrading of GET, these draft guidelines do not explicitly recommend an incremental approach, which is one of only two approaches consistently demonstrated to make a difference, and are used extensively in specialist clinics with good results. Suggestion: Please address and clarify these points.	experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. .The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise

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					programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. **With reference to Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion from evidence review G are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update

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Chartered Society of Physiotherapy	Guideline	028	012	Comment: We welcome that NICE recommend that patients ('who are able to and want to extend their physical activity') consult with a specialist therapist for a 'physical activity programme' (PAP). We absolutely support an incremental physical activity programme for people with ME/CFS, and we believe that the vast majority of patients have physical activity goals. These could include walking their children to school, sitting up for dinner, or might be more traditionally associated with 'exercise' like riding a bike or getting back to swimming. However, there is a lack of detail of what this is, what approach it uses, and how it can be implemented in clinical practice. Suggestion: Please provide further detail on the Physical Activity Plan. Please include information on content, development, patient collaboration, goal setting, progression / regression / stabilising.	Thank you for your comment. The recommendations at the end of this section set out the principles of a physical activity plan for a person with ME/CFS. The plan is collaborative and personalised and the detail of the plan would be specific to the individual.
Chartered Society of Physiotherapy	Guideline	028	016	Comment: Could the Committee please elaborate on what constitutes expertise in ME/CFS? We feel this requires further clarification as it will impact referral pathways, accessibility to services for people with ME/CFS, and whether physiotherapists feel confident enough to support this patient group. For example, are physiotherapists with speciality training in persistent/chronic pain considered to have the right skill set? Currently, this group of healthcare professionals commonly manage this patient group as there are only a limited number of services who specialise in managing people with CFS/ME. Suggestion: Clarify what constitutes training and expertise in ME. We suggest the following a. Specialist therapists should be trained in understanding ME/CFS and its symptoms, and more specifically trained in delivering appropriate physical activity programmes. This	Thank you for your comment. The committee note that there are occupational therapists and physiotherapists that work in ME/CFS specialist teams and have the specialist skills described in the guideline.

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				usually includes, but is not limited to, specialist physiotherapists and/or occupational therapists. b. Following the physical activity guidance as described here does not replace the need for specialist training, delivered by trainers with extensive experience in both ME/CFS and in the delivery of physical programmes for this patient group.	
Chartered Society of Physiotherapy	Guideline	028	019	Comment: The strong recommendation about physical activity / graded exercise therapy does not appear consistent with the limited evidence and variations in outcome (both beneficial and not), and suggest the recommendation should be softened. (and in supporting rationale p.63 L16) Suggestion: Alter phrasing at p28. L.20 to 'Take into account that….' Include a clarifying statement to describe physical activity programme, for example: 'that activity plans should be a tailored strategy, individualised, developed and adapted as needed with the person with ME/CFS to support self-management'	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).

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					GET Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases

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					in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. . The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
Chartered Society of Physiotherapy	Guideline	028	023	Comment: We agree with most of this section (1.11.20). However, as part of re-engaging with valued activities there is an element of unknown with regards to outcome. The role of physiotherapy is to support people with this, not necessarily to completely avoid adverse outcomes, as this is impossible. This could be interpreted that people should only engage in activities which are symptom-free and could result in people avoiding some activities out of fear of any adverse outcome. Sedentary time is associated with an increased risk of death compared to people who have a more active lifestyle (Ekelund et al 2020) Suggestion: The definition of adverse outcomes needs to be clarified. Additionally, alongside the discussions of potential benefits and harm from physical activity, the impacts of long-term inactivity should also be discussed. This information should be clearly and impartially presented to support informed decision making for people with ME/CFS. Ekelund, U., Tarp, J., Fagerland, M.W., Johannessen, J.S., Hansen, B.H., Jefferis, B.J., Whincup, P.H., Diaz, K.M., Hooker, S., Howard, V.J. and Chernofsky, A., 2020. Joint associations of accelero-meter measured physical activity and sedentary time with all-cause mortality: a harmonised meta-analysis in more than 44 000 middle-aged and older individuals. British Journal of Sports Medicine, 54(24), pp.1499-1506.	Thank you for your comment. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. As you note this is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly. *Long term inactivity* The physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.

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Chartered Society of Physiotherapy	Guideline	029	006 - 013	Comment: Further detail about setback management would be helpful,: Suggestion: We suggest you include something such as: Setback management: Setbacks are a normal part of any programme and should be normalised, explored, and managed appropriately according to the individual circumstances. Depending on the severity and cause of the setback, it may be appropriate to maintain physical activity if the patient feels able to and would like to do so, and to reduce any detrimental impacts caused by the activity reduction. It may also be appropriate to agree a temporary reduction in physical activity, increasing again to previous levels as soon as is sustainably possible.	Thank you for your comment. The recommendations include that the plan should include recognising a flare-up or relapse early and outlining how to manage it. This links to the section on flare-ups and relapses. In this section the committee have added a recommendation raising awareness that ,' that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed.'
Chartered Society of Physiotherapy	Guideline	029	017	Comment: Why has NICE left any information on sleep management out? Because of lack of evidence? It mentions sleep and rest briefly 1.11.23. and discusses rest but offers no advice on managing sleep, how poor sleep can impact on symptoms or how to regulate it or medications to help. Sleep management is a key component of treatment and should be included in the guide. Sleep hygiene, regulating sleep times, reducing daytime sleep as much as possible all help to increase the quality of sleep. Suggestion: Please consider adding more detail to this section about sleep hygiene, regulating sleep times, reducing daytime sleep as much as possible all help to increase the quality of sleep	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Chartered Society of Physiotherapy	Guideline	030	013	Comment: We were surprised to see no reference to the NICE guidance for managing chronic pain. Arguably, for this patient group, this guidance would be more appropriate than the guidance referenced for neuropathic pain and headaches. Suggestion: Please provide an evidence based justification for the selection of the guidelines that are referenced in this	Thank you for your comment. *Neuropathic pain and headaches* The committee disagree these references are inappropriate, people with ME/CFS report many different types of pain, neuropathic pain and headaches included. These are examples of NICE guidelines on pain and is not intended to be an

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				guideline. In addition, please add reference to the NICE guideline Chronic pain in over 16s: assessment and management.	exhaustive list of the types of pain people with ME/CFS may experience. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any symptoms or co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Chartered Society of Physiotherapy	Guideline	034	002	Comment: We agree with the first statement, in that CBT should be used to manage symptoms and the associated psychological distress. However, the statement 'do not offer CBT as a treatment or cure for ME/CFS' is misleading as in our experience CBT is never offered as a cure. Our concerns, as with the comments surrounding physical activity, is that these absolute statements may lead to blanket views about a particular approach, whereas in reality these are used in combination to support a person-centred, holistic rehabilitative approach for people with ME/CFS. Suggestion: Please remove this statement, as it does not reflect how CBT is used in routine clinical practice.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. Curative has been included in the recommendation to reflect the qualitative evidence (see evidence reviews A XX) and the committee's experience that people with ME/CFS had been directed towards CBT as a cure for ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Chartered Society of Physiotherapy	Guideline	036	001	Comment: It is stated that these guidelines will not cover all the symptoms that can occur in ME/CFS, specifically referring to other NICE guidelines. Should the committee not have said that the guidelines do not cover "all the symptoms that can occur if people have *co-morbidities* alongside their CFS/ME"? There are notable omissions in the guidance for co-existing conditions (IBS, Chronic Pain, Depression), is there a reason for this? Surely the NICE chronic pain guideline and the NICE IBS guideline would also be relevant to reference here? All of these guidelines recommend physical activity as a management strategy to improve symptoms, the opposite of what this guideline recommends. This is deeply confusing for clinicians and patients. Suggestion: Please include references to NICE guidance for chronic pain, IBS, headaches and depression. Please clarify whether physical activity (as recommended in these guidelines) should be implemented in patients with coexisting conditions?	Thank you for your comment, The NICE guideline on headaches in the over 12s is cross referred to in the' Managing pain' section of the guideline. The NICE guidelines on depression are cross referred to in the' Managing co-existing conditions' section of the guideline. *Irritable bowel syndrome guideline* The IBD guideline has been added to the list of NICE guidance in the co-existing conditions section of the guideline. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
Chartered Society of Physiotherapy	Guideline	049	018	Comment: There is a recommendation to start diagnosing CFS/ME at 6 weeks and therefore telling people to stay within their energy envelope from this time. The research shows that people have a better prognosis if treated using an early rehabilitation approach, and the committee actually recognise this on page 51 (line 5) (Candy et al. 2004 - https://doi.org/10.1016/S0022-3999(03)00370-2), rather than a pacing strategy. .	Thank you for your comment. To note 'provisional' diagnosis has been deleted. After considering the stakeholder comments the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. At 6 weeks ME/CFS is suspected and directed to the section on advice for suspected ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Chartered Society of Physiotherapy	Guideline	051	013	Comment: To suggest that providing the advice recommended in this guideline would not impose a significant cost on the NHS is not true. Advising people to stay within their energy envelope will not lead to fewer people with deteriorating symptoms. There is a risk of an increase in people feeling hopeless, and accumulating many other illnesses and symptoms that are linked not only with their ME/CFS but also with a sedentary lifestyle. In essence, people will get worse and need more help. Setting up home based MDTs for those severely affected will also bear a substantial cost, and one wonders what they will be able to provide to people with ME/CFS, especially as all recommendations for current evidence based approaches have been removed. This guideline will likely have profound costs for the NHS.	Thank you for your comment. After considering the stakeholder comments including those on the risk of early diagnostic labelling, the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are that provisional' diagnosis has been deleted. The committee agreed that the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. *Advice for people with suspected ME/CFS* The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. Taking into account the views of people with ME/CFS in the qualitative evidence the committee agreed it was important to make recommendations for support at this stage while acknowledging there is a lack of trial evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS. The committee agreed the advice would not be harmful in the short term either to people that are later diagnosed with ME/CFS or those that are diagnosed with another condition.
Chartered Society of Physiotherapy	Guideline	060	022	Comment: What seems to be recommended is that specialists have the expertise to support patients within their 'envelope' but not help people progress their envelope. This seems restrictive to the highly specialist clinicians who support their ME/CFS patients in a patient-centred and yet progressive way. It is even more unfair to patients, to provide little detail in how they can work with clinicians to try and improve their physical activity levels (if this is their goal). Imagine the psychological effect of being told you will never get better, since there are no available treatments for your condition?	Thank you for your comment. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits.

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					This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. (see evidence review G- self management strategies) In addition based on the quantitative and qualitative evidence (evidence reviews A, F,G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Chartered Society of Physiotherapy	Guideline	061	020 – 022 + 025	Comment: This section refers to the use of "tools" but does not provide clarity regarding what exactly these are or how they may be used. This ambiguity needs to be solved. Suggestion: Clarify this section and provide examples of tools that may be used (preferably from the evidence base or that have been tested in clinical practice) and that have detailed information on how they are implemented.	Thank you for your comment. The recommendation includes some examples but as the rationale states there is a lack of effectiveness evidence on tools and the committee were unable to make specific recommendations. In addition the committee made a research recommendations to address this.

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Chartered Society of Physiotherapy	Guideline	062	General	Comment: "In the committee's experience, people with ME/CFS have had varying results from physical activity programmes and they thought it was important to discuss this with people with ME/CFS and talk to them about the possible risks and benefits. The committee outlined what a personalised physical activity plan should look like based on their experience." Surely we cannot base a NICE guideline on the experience of the committee – surely the committee are there to look at the evidence not their own experiences as these will be anecdotal, and not science. The plural of anecdotes is not systematically acquired data.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Faculty of Homeopathy	Evidence review G	339	015	It is accepted that there is insufficient high quality or randomised control trial (RCT) evidence to support any NICE appraisal or recommendation for a range of complementary therapies for CFS. I am focusing on herbal medicines in this comment. Additionally, methodological problems exist with RCTs in herbal medicine. This is also because real world data would involve individualised herbal prescriptions, often with unique formulae or combinations for each patient. It can also be difficult to adequately blind the herbal medication – since typical dispensing	Thank you for your comment and information. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review.

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				as tinctures or granulated powders will often have a strong taste. Perhaps a methodology is a 3-arm trial with a standard herbal formula, a customised individual herbal formula, and a placebo/conventional treatment. Or with the limitations in time, funding and resources, perhaps research is best suited to carefully designed case cohorts and also outcomes based research, even though these are lower in the NICE evidence hierarchy (however, even the report by Helen Bell et al 2016 found selection bias and use of non-RCT evidence is sometimes necessary and NICE increasingly use Real World Data). Dalziel et al found in their review of 47 NICE Health Technology Assessment (HTA) Reports that 14 (30%) had included information from case series studies. I therefore suggest that NICE issue an Individual Research Recommendation for the question: Whether herbal medicine (western or Chinese) are safe and effective as adjunctive or support treatment for management of CFS. I note that NICE had issued a similar herbal medicine Research Recommendation (CG61/5) in Feb 2008 for irritable bowel syndrome, but perhaps a better response from the herbal industry will now be forthcoming. This is after all a growth field, with ethnobotanical research identifying many potentially active antinociceptive plant-derived active compounds (Joao Calixto et al 2005). Some relevant reviews on herbal research for national health systems can be listed: Helen Bell et al. The Use of Real World Data for the Estimation of Treatment Effects in NICE Decision Making. Report by the Decision Support Unit, ScHARR, University of Sheffield, 17th June 2016 (updated 12th Dec 2016). www.nicedsu.org.uk K. Dalziel et al. Do the findings of case series studies vary significantly according to methodological characteristics? Executive Summary. Health Technology Assessment 2005; Vol 9; No.2. doi: 10.3310/hta9020	In summary the effectiveness of medicines is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. The committee recognised the lack of research into any medicines but did not identify any one or type of medicine to prioritise for research and as such did not make any research recommendations on this topic.

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				Jon Tilburt & Ted Kaptchuk. Herbal medicine research and global health: an ethical analysis. Bulletin of the World Health Organization. August 2008, 86 (8) doi:10.2471/BLT.07.042820	
Faculty of Homeopathy	Guideline	General	General	[2.1.5.8 Narrative summary of review findings for adults (severity mixed or unclear) who have had alternative therapies] The Narrative summary rightly highlights important qualitative findings including –a frustration at lack of NHS or private health insurance funding for complementary therapies for CFS/ME and the value of a holistic approach and regular follow up. The draft guidelines reflect the need for, and interest in holistic approaches to management. The guidelines find mixed evidence in evaluations of complementary therapies; some were found to be helpful and should inform further areas of research. The statement 'not enough robust evidence to recommend any type of complementary therapy' does not equate to evidence of absence of efficacy. The reason for exclusion of many studies is methodology limitations and the review highlights a need for larger, well designed trials appropriate to the therapeutic intervention. Clinical and observational studies are better able to assess the effect of complex interventions in real world practice. Future research should include mixed methodology approaches with pragmatic design and qualitative studies. The use of complementary therapies as an individualised treatment can be experiential, intuitive and holistic.	Thank you for your comment and information. The committee agree that there is need for well-designed trials evaluating the clinical and cost effectiveness of interventions for people with ME/CFS.
Faculty of Homeopathy	Guideline	011	015	I agree with the emphasis on holistic assessment of CFS patients. CSF is complex, multisystem condition with symptoms that vary in nature and severity and so support the need for an individualised and holistic approach in management and self-care. There is also a clear need for the NHS to improve access to Integrative Medicine (IM) specialist ME/CFS services. An Integrative Medicine doctor/practitioner can help a person develop an individualised treatment plan, based on their needs, while also building trust and relationships over time. More than	Thank you for your comment and information. Recommendation 1.5.2 is to develop and agree a personalised care and support plan. To note, management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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				one treatment modality can be combined with support from a multi-disciplinary team of complimentary and health care practitioners. Integrative Medicine is founded on ideas of holism and individualism. NHS Centres for Integrative Medicine already provide specialist holistic CFS services focused on complementary therapy approaches and self-care. The services have high levels of patient satisfaction and engagement, with the Centre for Integrative Care in Glasgow recognised as a centre of excellence in person-centred care. https://www.uclh.nhs.uk/our-services/find-service/integrated-medicine/chronic-fatigue-syndrome-cfs-service https://www.nhsggc.org.uk/patients-and-visitors/main-hospital-sites/gartnavel-campus/nhs-centre-for-integrative-care/nhs-centre-for-integrative-care-therapies/holistic-chronic-fatigue-syndromeme-service/ The committee excluded various studies in complementary therapies with reliance being weighted heavily on high quality RCT, this is at variance with the needs of clinicians in the real world. Hierarchical model of evidence, are not perhaps the appropriate tools to evaluate complex interventions where internal and external validity of RCT trial design is problematic. A whole systems research model is a proposed alternative with epistemologically sensitive methodology to establish pragmatic and rigorous evidence for complex interventions.[1] [2] [1] Verhoef MJ, Lewith G, Ritenbaugh C, Boon H, Fleishman S, Leis A. Complementary and alternative medicine whole systems research: beyond identification of inadequacies of the RCT. Complementary therapies in medicine. 2005 Sep 1;13(3):206-12. https://doi.org/10.1016/j.ctim.2005.05.001 [2] Walach H, Falkenberg T, Fønnebø V, Lewith G, Jonas WB. Circular instead of hierarchical: methodological principles for the	*Excluded studies* All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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				evaluation of complex interventions. BMC medical research methodology. 2006 Dec;6(1):29. Doi:10.1186/1471-2288-6-29	
Faculty of Homeopathy	Guideline	024	004	A survey of your draft evidence reviews of both pharmacological and non-pharmacological management of CFS does not sufficiently appraise the possible role of herbal medicine. A significant herbal strategy for managing CFS is use of adaptogens, which are herbal medicines that promote general resistance to stress and are typically regarded as restoratives and tonifying herbs. The most extensively studied for CFS are *Rhodiola rosea*, *Eleutherococcus senticosus* and *Schisandra chinensis*. Indeed, ADAPT-232 (Chisan), a fixed combination of R rosea, E senticosus, and S chinensis has been used in Scandinavia since 1979 for decreased performance, fatigue, and weakness. A review article may be found in: Alexander G. Panossian, Adaptogens in Mental and Behavioral Disorders. Psychiatr Clin N Am 36 (2013) 49–64. http://dx.doi.org/10.1016/j.psc.2012.12.005 A definition of adaptogen is provided in: EMEA/HMPC/102655/2007. Reflection paper on the adaptogenic concept. London: European Medicines Agency; 2008. Of note it is mentioned in this document that adaptogen herbs can be distinguished from herbal stimulants in that the former are reputed to increase work capacity without a subsequent decrease in performance or rebound exhaustion. It is accepted that there are shortcomings in the clinical research evidence and more work is needed to further the concept of adaptogen. It is of merit therefore to at least include a recommendation (within the draft guideline page 46 'Other recommendations for research') for further assessment to be included on herbal management with a particular focus on herbs used in traditional herbal medicine, or an established body of evidence for use.	Thank you for your comment. Complementary and alternative therapies were included in the protocol for non- pharmacological interventions and when reviewing the evidence the committee agreed that there is insufficient evidence to recommend any complementary approaches.

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Faculty of Homeopathy	Guideline	024	004	There are a myriad of herbal diagnoses and treatment strategies (for example in both western herbal medicine and Traditional Chinese Medicine) to treating ME/CFS, but of course randomised controlled trials and meta-analyses may not be presently evident to a great degree. Examples from a sample search include: J.H. Cho et al. Myelophil, an extract mix of Astragali Radix and Salviae Radix, ameliorates chronic fatigue: A randomised, double-blind, controlled pilot study. Complementary Therapies in Medicine (2009) 17, 141-146. doi:10.1016/j.ctim.2008.11.003 from the abstract: Objectives: To investigate the anti-fatigue effects of Myelophil, an extract of a mix of Astragali Radix and Salviae Radix, which has been used to treat patients with chronic fatigue. Subjects and design: A randomised, double-blind, controlled clinical trial was performed with 36 adults who complained of chronic fatigue. The subjects were divided among a control group and low- and high-dose groups (3 or 6 g of oral Myelophil per day, respectively) and were monitored for 4 weeks. Fatigue severity was subjectively characterised, and the expression of 42 cytokines was evaluated using an antibody array. Results: Myelophil administration (3 g per day) significantly decreased the fatigue severity score compared with the control ($p < 0.05$). No changes were noted in cytokine expression. Conclusions: Myelophil appears to have a pharmacological effect against fatigue, suggesting the clinical relevance of the traditional medicinal plants, Astragalus membranaceus and Salvia miltiorrhiza. A paper on Myelophil is appraised in your page 27 of the evidence document `[G] Evidence reviews for the non-pharmacological management of ME/CFS`, with a full analysis on page 172-173. However, in real world herbal prescribing, there is fine tuning of herbal formulae with additional or substituted ingredients depending on an individualised case assessment of	Thank you for your comment. Complementary and alternative therapies were included in the protocol for non- pharmacological interventions and when reviewing the evidence the committee agreed that there is insufficient evidence to recommend any complimentary approaches.

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				the patient's health symptoms, history and examination. Rather than excluding herbal medicine as an important management tool for CFS, it is pertinent to advocate this as a research recommendation. Yu-Yi Wang et al. Traditional Chinese medicine for chronic fatigue syndrome: A systematic review of randomized clinical trials. Complementary Therapies in Medicine (2014) 22, 826-833. http://dx.doi.org/10.1016/j.ctim.2014.06.004 from the abstract: Background: There is no curative treatment for chronic fatigue syndrome (CFS). Traditional Chinese medicine (TCM) is widely used in the treatment of CFS in China. Methods: We searched six main databases for randomized clinical trials (RCTs) on TCM for CFS from their inception to September 2013. The Cochrane risk of bias tool was used to assess the methodological quality. Results: 23 RCTs involving 1776 participants were identified. The risk of bias of the included studies was high. The types of TCM interventions varied, including Chinese herbal medicine, acupuncture, qigong, moxibustion, and acupoint application. The results of meta-analyses and several individual studies showed that TCM alone or in combination with other interventions significantly alleviated fatigue symptoms as measured by Chalder's fatigue scale, fatigue severity scale, fatigue assessment instrument by Joseph E. Schwartz, Bell's fatigue scale, and guiding principle of clinical research on new drugs of TCM for fatigue symptom. There was not enough evidence that TCM could improve the quality of life for CFS patients. The included studies did not report serious adverse events.	
Faculty of Homeopathy	Guideline	024	014	Incorporating Mindfulness within Energy management systems should be explicitly stated. I argue that mindfulness is implied in the very nature of energy management, since the patient is encouraged to become aware of their own energy, including ingrained and behavioural patterns. For many patients, it would be difficult to develop their own set of mindfulness tools without	Thank you for your comment. No evidence was identified that evaluated incorporating mindfulness with energy management and the committee focused on the principles of energy management in this section.

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				the help of a specialist. Many reviews of Energy Management Systems do not include any details on fostering mindfulness. For example the paper by: A. Vatwani, R. Margonis. Information/Education Page: Energy Conservation Techniques to Decrease Fatigue. Archives of Physical Medicine and Rehabilitation 2019;100;1193-6. https://doi.org/10.1016/j.apmr.2019.01.005 is a very useful summary of the main components of energy management, but does not mention mindfulness. I have expanded on this point in my comment to page 34, line 1.	
Faculty of Homeopathy	Guideline	027	024	Although not curative, there are nonetheless various physical therapies that encompass mindfulness and bodily awareness of one's own energy envelope, which would be therefore fully compatible and augment an Energy Management System. A particular example, and which should perhaps be included as a research recommendation, is Qigong (Chi Kung). There are many papers on the use of Qigong within the Chinese Medicine literature, since it is an integral component of a whole-person centred approach to many disease conditions as well as health promotion. A paper of focus for fatigue treatment is: Rainbow T. H. Ho et al. A Randomized Controlled Trial of Qigong Exercise on Fatigue Symptoms, Functioning, and Telomerase Activity in Persons with Chronic Fatigue or Chronic Fatigue Syndrome. Ann. Behav. Med. (2012) 44:160–170. DOI 10.1007/s12160-012-9381-6 From the abstract: Purpose: To assess the effect of a 4-month qigong intervention program among patients with chronic fatigue syndrome. Methods 64 participants were randomly assigned to either an intervention group or a wait list control group. Outcome measures included fatigue symptoms, physical functioning, mental functioning, and telomerase activity. Results Fatigue symptoms and mental functioning were significantly improved in the qigong group compared to controls. Telomerase activity increased in the qigong group from 0.102 to 0.178 arbitrary units ($p<0.05$). The	Thank you for your comment. No evidence was identified to support recommending physical therapies that encompass mindfulness and bodily awareness for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on this.

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				change was statistically significant when compared to the control group (p<0.05). Conclusion Qigong exercise may be used as an alternative and complementary therapy or rehabilitative program for chronic fatigue syndrome.	
Faculty of Homeopathy	Guideline	031	010	There are major effectiveness gaps in the conventional treatment of CSF. The guidelines are right to highlight how people with ME/CFS may be more intolerant of drug treatment and have more severe adverse effects. In contrast evidence shows complimentary therapies are safe and helpful in chronic conditions. For example, the number of serious Adverse Drug Reactions from herbal medications is small compared to conventional medicine. Posadzki P, Watson LK, Ernst E. Adverse effects of herbal medicines: an overview of systematic reviews. Clinical medicine. 2013 Feb 1;13(1):7-12. Doi: 10.7861/clinmedicine.13-1-7 Dantas F, Rampes H (2000). Do homeopathic medicines provoke adverse effects? A systematic review. Br Homeopath J. 89:S35–38. Doi: 10.1054/homp.1999.0378	Thank you for your comment and this information.
Faculty of Homeopathy	Guideline	034	001	Mindfulness should be included as a key psychological management for CFS. It may assist as a stand-alone tool, but especially facilitates a more successful implementation of an energy management system, personalised for each individual. An example trial that studied the efficacy of mindfulness for CFS is: Lone Overby Fjorback et al. Mindfulness therapy for somatization disorder and functional somatic syndromes - Randomized trial with one-year follow-up. Journal of Psychosomatic Research 74 (2013) 31–40. http://dx.doi.org/10.1016/j.jpsychores.2012.09.006 The study defined bodily distress syndrome BDS as a range of conditions and included Chronic Fatigue Syndrome CFS, the conditions having sub-group analysis. From the abstract	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). We note the study you reference is not specific to a ME/CFS population and it is unclear how may people included where diagnosed with M/CFS or how they were diagnosed with ME/CFS.

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				The study randomized 119 patients to either mindfulness therapy (mindfulness-based stress reduction and some cognitive behavioral therapy elements for bodily distress syndrome BDS or to enhanced treatment as usual (2-hour specialist medical care and brief cognitive behavioral therapy for BDS). The primary outcome measure was change in physical health (SF-36 Physical Component Summary) from baseline to 15-month follow-up. Results: The study is negative as we could not demonstrate a different development over time for the two groups (F(3,2674)=1.51, P=.21). However, in the mindfulness therapy group, improvement was obtained toward the end of treatment and it remained present at the 15-month follow-up, whereas the enhanced treatment as usual group achieved no significant change until 15-month follow-up. The change scores averaged half a standard deviation which amounts to a clinically significant change, 29% changed more than 1 standard deviation. Significant between-group differences were observed at treatment cessation. Conclusion: Mindfulness therapy is a feasible and acceptable treatment. The study showed that mindfulness therapy was comparable to enhanced treatment as usual in improving quality of life and symptoms. Nevertheless, considering the more rapid improvement following mindfulness, mindfulness therapy may be a potentially useful intervention in BDS patients. Clinically important changes that seem to be comparable to a CBT treatment approach were obtained.	
Faculty of Homeopathy	Guideline	034	016	A discussion of illness belief systems should include any co-morbid depression and/or anxiety. In the systemic review paper cited below, around 36% - 70% of patients experience clinical levels of depression and 32% - 57% experience clinical levels of anxiety. If these states are not also addressed, there is likely to be a poorer prognosis and relapse after treatment. Furthermore,	Thank you for your comment and information.

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				understanding modifiable psychological processes linked to anxiety and depression in CFS/ME facilitates more effective interventions. In particular 'Perfectionism' has been found to be an important determinant. This state has been measured in different ways. For example Hewitt and Flett's Multidimensional Perfectionism Scale (MPS-H) and The Almost Perfect Scale-Revised (APS-R). Amelia Wright et al. Perfectionism, depression and anxiety in chronic fatigue syndrome: A systematic review. Journal of Psychosomatic Research 140 (2021) 110322. https://doi.org/10.1016/j.jpsychores.2020.110322	
Faculty of Homeopathy	Guideline	034	030	I agree with the components of the CBT advised only for ME/CFS patients, who would like to use it to support them in managing their symptoms. An additional component should utilise approaches of mindfulness, which often involves various psychotherapeutic approaches but also teaching meditation techniques. To quote from one paper. The aim of this systematic review was to assess the effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome (CFS). Imke Courtois et al. Effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome: A systematic review and meta-analysis. Journal of Bodywork & Movement Therapies (2015) 19, 35e56. http://dx.doi.org/10.1016/j.jbmt.2014.04.003 CFS (and fibromyalgia) may remain frustrating because a substantial subgroup of patients may need a more holistic therapeutic approach, including experiential/psychodynamic and systemic psychotherapy, and/or adequate psychopharmacological support. In addition to physical symptoms patients often complain of lack of confidence and trust in their body along with feelings of depression and/or anxiety. Furthermore, body awareness can be defined as "the	Thank you for your comment and information. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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				subjective, phenomenological aspect of proprioception and interoception that enters conscious awareness, and is modifiable by mental processes including attention, interpretation, appraisal, beliefs, memories, conditioning, attitudes and affect. In the past clinicians assumed that an increased body awareness would lead to somatosensory amplification, more severe anxiety symptoms, hypochondria and thus an unfavourable clinical outcome (such as more pain). However, in a new physiotherapeutic context, body awareness has a twofold definition: (1) the experience of the body (i.e. experience dimension) and (2) the actions and behaviour in movements and activities (i.e. movement dimension). In 'movement dimension', the body awareness therapy aims to normalize posture, balance, breathing and muscular tension or stiffness which are visible and experienced in the movement pattern.	
Forward-ME	Guideline	General	General	Members of Forward-ME are, on the whole, extremely pleased with the tone and content of the Draft Guideline and would like to thank all those who have contributed to the development for their role in listening to the concerns of the community and for their understanding of the misconceptions faced by people with ME/CFS over many years and for coming to grips with a very difficult problem. We remain concerned about the use of 'chronic fatigue syndrome' (CFS) as many patients who have chronic fatigue do not have ME as is shown in section G. Our preferred term is 'ME'. Plausible hypotheses as to possible underlying causes have emerged from the observed pattern of illness and the wide range of physical abnormalities that have been documented for some time. This information has not yet been drawn together to produce an inclusive and conclusive picture of the reasons behind the onset and persistence of ME in each and every case.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*

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				However, it is highly misleading to imply that there are not, at a minimum, some very strong clues as to what is going on.	
Forward-ME	Guideline	001	016	We understood this would be a new guideline to *replace* guideline G53 and not an update. Please clarify.	Thank you for your comment. This has been edited to, 'this Guideline will update and replace NICE Guideline CG53 (published August 2007)'.
Forward-ME	Guideline	004	005	Delete 'medical condition'. Insert 'disease' Reason: ME/CFS is a recognised neurological disease. Benign myalgic encephalomyelitis is classified by the World Health Organisation International Classification of Disease 10 (WHO ICD 10) at G93.3 (other disorders of the nervous system). The forthcoming ICD 11 maintains this classification, listing chronic fatigue syndrome there also. This classification is recognised by the Department of Health and Social Care. It is also recognised as a disease by all of the United States (US) authorities and by many researchers. It would be consistent if the term 'disease' is used throughout in place of 'medical condition' which appears to diminish the impact of ME/CFS. We are aware of the view that 'multi-system' is appropriate and the term 'complex' redundant. If NICE wish to retain the term 'complex' in the guideline, please clarify what this implies.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease and keep complex, to indicate ME/CFS is multifaceted and complicated. Reference to the ICD10 classification has been included in the context section of the guideline.
Forward-ME	Guideline	004	015 onwards	Add: It should not be confused with medically unexplained symptoms (MUS) or with functional neurological disorder (FND). Reason: Without these specific exclusions in the guideline, clinicians will see no need to change the current practice of misconstruing ME/CFS as MUS or FND. Other NICE materials direct them to do so and there is an urgent need for these to be updated to specifically exclude ME/CFS. For example, the Suspected Neurological Conditions Guideline NG127, in the section linking recommendations to evidence – recommendation 38 and under heading *Chronic fatigue syndrome, fibromyalgia and functional neurological disorder* , and the current Improving Access to Psychological Therapies (IAPT) manual, updated in March 2020, defines MUS with the example of chronic fatigue syndrome.	Thank you for your comment. This section of the guideline raises awareness about what ME/CFS is and not what it isn't. The section on 'suspecting ME/CFS' has further details on how to diagnose ME/CFS and emphasises is the importance of excluding other diagnoses. For this reason your suggestion has not been added to the recommendation.

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Forward-ME	Guideline	004	021 onwards	Ensure that at every stage, patients must be fully informed of all the benefits and risks of procedures or treatment and that their consent is obtained. In the case of children, the parent or carer should consent.	Thank you for your comment. The committee agree that the issue of consent and choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person/child centered care is directly reinforced in the guideline sections 'approach to delivering care' and 'assessment and care planning'. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Forward-ME	Guideline	005	002	Delete 'should'. Insert 'must'. Reason: It is essential that health and social care professionals have a clear-cut understanding of ME/CFS in order to prevent harm. This requirement might incur training costs, but we are of the view that the savings in additional medical and social care costs would outweigh them in the long term.	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. The guideline reflects the evidence for best practice. There committee acknowledge there are that may need support and investment, such as training costs, to implement some recommendations in the guideline.
Forward-ME	Guideline	005	002 onwards	Insert new bullet point: a person diagnosed with ME/CFS or suspected of having ME/CFS may experience brain fog/cognitive challenges and a longer appointment time may need to be scheduled. Reason: executive function challenges that come under cognitive difficulties can often be both taxing and exhausting for patients	Thank you for your comment. Access to care is addressed in detail in section 1.8 and includes your suggestions.

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				during medical/social care/benefits appointments. Patients struggle to share, follow and process conversations or share and, at that time, remember historic details important to their medical outcomes, management and support.	
Forward-ME	Guideline	005	008	Add: Ensure that at every stage, patients must be fully informed of all the benefits and risks of procedures or treatment and that their informed consent is obtained. In the case of children, the parent or carer should consent. Ensure that they fulfil their legal obligations when securing informed consent. *I.e.*, patient made aware of any material risks involved in any recommended treatment (Montgomery vs Lanarks Health Board 2015 UK Supreme Court Judgement 11)	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Forward-ME	Guideline	005	012	We are particularly pleased to see this. It would maintain connection between the patient and their registered medical practitioner to the benefit of the patient and would enhance awareness of the disease to the doctor. It would also overcome the inability of patients to provide medical evidence for insurance, out of work and disability claims, and welfare benefits claims and would be likely to produce savings to the public purse if decisions are right first time.	Thank you for your comment.
Forward-ME	Guideline	005	013	After 'changing' insert 'or the patient is housebound or has co-morbidities. In a case where a patient has both a domiciliary visit is necessary.	Thank you for your comment. This recommendation refers to the review and includes all people with ME/CFS. The access to care section provides information on how to support people with ME/CFS to access care.
Forward-ME	Guideline	005	014 onwards	Recognise that ME/CFS is a disability protected under the Equality Act 2010 and act accordingly.	Thank you for your comment. In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.

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Forward-ME	Guideline	005	018 onwards	It would be helpful to have a 'Management and Support Plan'. The Management part would be to manage the disease and the Support part would be for the support of the patient. Reason: Because of the fluctuating nature of ME/CFS, Forward-ME are concerned that the terms of the Management Plan may be too inflexible. It is unlikely in the near future that there will be a 'specialist team' as envisaged by the guideline, to prepare a plan with the patient.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.).
Forward-ME	Guideline	005	019	The whole of this section is very welcome. A proper understanding of ME/CFS should result in reduced administration and litigation costs to the NHS and local authorities.	Thank you for your comment.
Forward-ME	Guideline	006	007	This section is also most welcome as it should help health and social care professionals to understand the more severe manifestations of the disease. It makes clear to hospital staff the particular needs of the severely affected should they need admission to hospital. While it is not the primary purpose of the guideline, it should also help DWP officials and healthcare professionals employed by the disability assessing agencies to gain enhanced understanding which could result in cost savings for benefit reviews and appeals if decisions are correct in the first instance.	Thank you for your comment.
Forward-ME	Guideline	007	004	Delete 'may'. Insert 'are likely to'.	Thank you for your comment. The level of support needed is individual to the person and agreed as part of their personalised care and support plan. As such 'may' is appropriate in this context.
Forward-ME	Guideline	008	009 onwards	Add bullet point: 'Be aware that misdiagnosis is relatively common and cases of serious but treatable diseases are missed.' There need to be more detailed differential diagnoses in this section.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the

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					importance of using clinical judgment when deciding on additional investigations. In addition, the committee discuss misdiagnosis in the discussion section of Evidence review D- Diagnosis and include a list of differential diagnosis and conditions that commonly occur in people with ME/CFS and has the examples you have listed.
Forward-ME	Guideline	008	009	It would be helpful if this point could be expanded to clarify appropriate baseline investigations as it was in the 2007 NICE Guideline CG53. It would be even more helpful to have a further section on specialist investigations relevant to ME/CFS. Unless and until patients are investigated the risk of a 'nothing physically wrong, label sticking like glue remains.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Forward-ME	Guideline	009	001	Box above - First line of bullet point: after 'problems' insert 'processing' Third line of bullet point: Delete 'confusion'. Insert 'uncertainty' Reason: Confusion may be interpreted as a lack of mental capacity	Thank you for your comments. The committee do not agree that processing adds any further clarity to the bullet points and for this reason have not added your suggestion. Confusion has been deleted from the bullet point.
Forward-ME	Guideline	009	004	As there is no specific NICE guidance for orthostatic intolerance to refer on to, the content here is insufficient. Be aware of postural tachycardia syndrome (PoTS), neurally mediated hypotension and orthostatic hypotension. Patients should be referred to a specialist with an interest in orthostatic intolerance. Consider providing compression hosiery and increasing salt and fluid intake whilst awaiting specialist input.	Thank you for your comment. The management of symptoms section in the guideline includes further recommendations on orthostatic intolerance.

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Forward-ME	Guideline	009	006 onwards	Add: Bullet point 'dysautonomia'.	Thank you for your comment. As with all examples included in recommendations they are not intended or can hope to be an exhaustive list. The committee note that the definition of orthostatic intolerance linked to includes further explanation.
Forward-ME	Guideline	011	007 - 008	We remain concerned that there is a dearth of consultant specialists in this field. As there is, currently, no effective treatment we consider that general practitioners (GPs) should take responsibility for their patients with ME/CFS. We would encourage specialist doctors and nurses to train within each GP practise. Approved distance-learning programmes are already available. Patients should be offered specialist consultant referrals if they choose.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. Based on the evidence (see evidence report I) and in the committee's experience clinicians working within a ME/CFS specialist team are the best healthcare professionals to develop a care and support plan, they have the expertise in ME/CFS and the understanding of the detailed assessment required at this stage. For this reason the committee have recommended that diagnosis and the development of the care and support plan should be carried out by a ME/CFS specialist team. Any clinician not working in collaboration with and supported by a ME/CFS specialist team should not be developing the care and support plan. The committee agree that review of the care and support plan can take place in primary care and this is set out in the review in primary care section of the guideline.

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					Throughout the guideline where it is relevant that specific expertise from a ME/CFS specialist team is needed this is recommended. For example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. *Training* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Forward-ME	Guideline	011	007	After 'management' insert 'and support'	Thank you for your support. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Forward-ME	Guideline	011	008	After 'management' insert 'and support'. It would be helpful to have a Management and Support Plan. The Management part would be to manage the disease and the Support part would be to support the patient.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Forward-ME	Guideline	011	009	In view of the current shortage of specialist ME/CFS paediatric specialist teams, and as diagnosis can be made on the clinical history, advice sometimes may be sought from a specialist ME/CFS paediatrician remotely after the GP has done the basic investigations to exclude other conditions.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development

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					of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Forward-ME	Guideline	012	010	After 'management' insert 'and support' and carry through the implications for the proposals currently set out in section1.5.2 - 1.5.4 and developed in late sections of the draft.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Forward-ME	Guideline	014	016	Delete 'medical condition'. Insert 'disease'	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease.
Forward-ME	Guideline	014	018	At the end insert: 'and are worsened by exertion'	Thank you for your comment. This recommendation is to give an overview of ME/CFS and there is more detail throughout the guideline on aspects of ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later in the energy management section of the guideline and for this reason your suggestion has not been added to the recommendation.
Forward-ME	Guideline	015	010	Delete 'condition'. Insert 'disease'	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After

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					discussing in detail the wording of this recommendation the committee agreed not to change condition for disease.
Forward-ME	Guideline	016	006 - 011	Replace 2 paragraphs with the following: 1.7.1 Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect. 1.7.2 Safeguarding assessments in people with confirmed or suspected ME/CFS, if needed, should be carried out and overseen by health and social care professionals who have training and experience in ME/CFS.	Thank you for your comment. Taking into account the range of stakeholder comments the recommendations in this section have been reordered. This has addressed the point you make about the order. The committee discussion in Evidence review B includes in detail why the recommendations on safeguarding have been included in the guideline and this refers to the lack of understanding and disbelief that parents have experienced.
Forward-ME	Guideline	016	016 onwards	Be aware that ME/CFS in children should not be mistaken for very rare conditions such as Munchausen's syndrome by proxy or with fabricated or induced illness	Thank you for your comment. This recommendation describes circumstances that may be mistaken for abuse and neglect for this reason your suggestion has not been included.
Forward-ME	Guideline	018	018 onwards	Insert new bullet point: 'they may have prepared prior to an arranged appointment by remaining completely inactive for some time'	Thank you for your comment. This recommendation raises awareness about the reasons people may miss an appointment not about preparation for an appointment and for that reason your suggestion has not been added.
Forward-ME	Guideline	019	001	Add: 'take into account 1.1.8 and discuss …….'	Thank you for your comment. Reference to 1.8.1 is included above the recommendation and inpatient has been added.
Forward-ME	Guideline	019	017	After 'management' add 'and support'	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Forward-ME	Guideline	021	005	At end add: 'full or part time. Return to these activities is likely to be gradual, if possible at all. Pushing to continue to work or attend school or further education is likely to result in lasting illness and disability.'	Thank you for your comment. In reference to providing specific details in the recommendations the committee note that any advice would be personalised and relevant to the person and have not added your suggestion.

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Forward-ME	Guideline	023	004	At end add: 'if and when able'	Thank you for your comment. This recommendation refers to the expertise that should be available and does not make any judgement about if someone needs the expertise. For this reason your suggestion has not been added.
Forward-ME	Guideline	023	009	After 'management' add 'and support'.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Forward-ME	Guideline	031	014 onwards	Insert new bullet point: 'avoid giving a further drug to counter side effects.'	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
Forward-ME	Guideline	037	001 - 024	Forward-ME are very pleased to see these two sections so clearly expressed	Thank you for your comment.
Forward-ME	Guideline	040	012	Delete 'should'. Insert 'must'	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
Forward-ME	Guideline	041	002	Delete 'should'. Insert 'must'.	Thank you for your comment. Must is used in a recommendation when there is a legal duty to apply a recommendation. This is not the case here and no changes have been made to the recommendation.
Forward-ME	Guideline	043	003 - 008	We hope that this definition will be expanded to include management (of the illness) and support (of the patient) as per comment 21. We are extremely concerned that any such plan should not always and automatically form the basis for all other assessment plans.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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Forward-ME	Guideline	034 + 035	General	In the evidence review at G Page 342 Line 26, the committee summarised the evidence on non-pharmacological interventions for ME/CFS. Their conclusions (from lines 40 – 44) found that: "In addition, the committee made 'do not' offer recommendations for CBT ………to treat or cure ME/CFS." In the light of this finding, Forward-ME are mystified as to why the draft guideline discusses CBT extensively. This would appear to be discriminatory as the guideline for multiple sclerosis (MS) – a disease that has been compared to ME/CFS, at 1.5.5 states only: 'Consider mindfulness-based training, cognitive behaviour therapy or fatigue management for treating MS-related fatigue. Congestive heart failure- also compared with ME/CFS only makes reference to Depression with reference to the NICE guideline on that topic. We can find no other chronic disease for which such extensive advice is given on CBT. We are aware that some patients may find psychological support necessary and helpful. CBT is mentioned as having two possible purposes: (1) Support in managing symptoms. CBT is only ever relevant when a person is behaving in a maladaptive fashion, grounded in unhelpful beliefs; therapist aims to change mindset to their benefit in terms of changed behaviour. (2) CBT for support with psychological distress as far as we are aware does not exist. Person-centred supportive counselling would be fit for purpose. We are asking for this section to be re-written to state: 'Do not offer CBT to treat or cure ME/CFS as there is no substantive evidence that it is effective. Patients may find supportive, person-centred counselling helpful.''	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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Healthwatch Kirklees	Guideline	General	General	The majority of the conversations Healthwatch Kirklees has had with our local ME/CFS support group have shown the difficulties in regards to GET and accessing this service. They would like to see other alternative treatment options and the removal of GET from NICE guidance but also treatment or support which is of a local nature. The current pathway for Kirklees is in Leeds which can take more than an hour to access via transport from some areas of Kirklees.	Thank you for your comment and information. The committee agree there is inequity in accessing services and that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Healthwatch Kirklees	Guideline	014	017	Feedback from ME patients in Kirklees has suggested that adaption to the wording of the guidance to include "provide evidence-based content developed by and in collaboration with; Practicing ME Physicians and Paediatricians who take a biomedical approach towards ME/CFS, Medical professionals who have ME/CFS, especially those who also have expertise in Medical Education and ME/CFS patient organisations".	Thank you for your comment. The committee agreed that up-to-date information uses plain language to describe 'evidence-based content. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Healthwatch Kirklees	Guideline	040	012	From working extensively in partnership for the past 4 years with our local ME/CFS support group they feel that training for health and social care professionals should be included within all physician curriculums and within this guidance with particular note of: ME/CFS should be included in the undergraduate medical curriculum, and postgraduate Physician, Paediatric and General Practice curriculums. All doctors should understand that ME/CFS is a complex, multi-system, chronic medical illness, not a psychological or psychiatric condition. It is classified by the World Health Organisation and by SNOMED-CT as Neurological. They hope that in the future all Physicians, Paediatricians and General Practitioners must be competent diagnosing and managing ME/CFS. This is due to groups multiple negative	Thank you for your comment. It is beyond the remit of NICE to recommend what should be included in medical curricula.

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				experiences of NHS services and negative feedback relating to current understanding and knowledge from NHS professionals most doctors within our locality believe ME/CFS is psychological and patients have been forced to access private medical treatment and diagnosis.	
Healthwatch Kirklees	Guideline	045	023	Through numerous conversations the group of patients that we have worked with they have provided insight into their opinion of underfunding for the ME/CFS conditions. They feel that Biomedical research into ME/CFS is urgently needed to unravel the pathophysiology and causation of ME/CFS, find reliable biomarkers and identify accurate diagnostic tests that can be made easily accessible in the clinical setting and to find effective treatments. They have told us that funding for biomedical research must be significantly increased commensurate with the disease burden of ME/CFS (250,000 patients in the UK) compared to other diseases such as MS. Particularly that funding for biomedical research into ME/CFS should be increased even further to catch up with 30 years of gross under funding and to move forward scientific understanding, diagnosis and treatments for people with ME/CFS.	Thank you for your comment. Research recommendations can only be made for where the evidence has been searched for within the guideline. Biomedical research was not included in the scope of this guideline as a topic to consider, and therefore we are unable to make research recommendations on this topic.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	General	General	We are concerned about the care pathway model outlined with reliance on specialist teams because: - The majority of existing specialist teams are not fit for purpose because: - Inappropriate staffing: many are led by Psychiatrists or Psychologists instead of Physicians, Paediatricians or General Practitioners. This is inappropriate as ME/CFS is a complex, multi-system, chronic medical condition. • The majority of current specialist clinics work on the theory of deconditioning and promote outdated and harmful treatments (GET and CBT). - Patients with moderate ME/CFS will struggle physically and financially to get to specialist centres unless they are local. In addition, patients with severe and very	Thank you for your comment. *Service design* This guideline focused on clinical care and service delivery was not included as part of the scope of the guideline and the committee are unable to make recommendations on the design of services. *Skills* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				severe ME/CFS will require home visits and this is much more difficult to facilitate from a regional specialist service as opposed to a local service. - It is likely that specialist centres will struggle to meet the needs of the volume of ME/CFS patients. - Caution is required to ensure that any specialist services empower GPs and local physicians rather than disempower them. We propose that: - Any existing specialist centres staffed by psychiatrists or psychologists as the primary staff members should be scrapped. All specialist services must be led by physicians, paediatricians or general practitioners with special interest. - Any existing specialist centres operating on the understanding that ME/CFS is due to dysfunctional illness beliefs and deconditioning should be scrapped. An urgent educational campaign must be commenced to re-educate healthcare professionals on ME, starting with any staff who will be involved in ME services, and including all physicians, paediatricians, general practitioners, mental health workers (to avoid misdiagnosis or inappropriate management), occupational therapists, physiotherapists, nurses and social workers. - All Physicians, paediatricians, general practitioners and advanced nurse practitioners, should be made competent in diagnosing and managing ME/CFS, and should take ownership of their ME/CFS patients - Any specialist services should be local and community-based with the capacity to handle the volume of ME/CFS patients in that local area, and the ability to perform sufficient home-visits for patients with severe and very severe ME/CFS.	. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agree that there is variation in the delivery of home visits across the NHS but these recommendations will provide equity of access for this group, particularly for people with ME/CFS who are have difficulty or are unable to leave their homes.. *Quality and Outcomes Framework* It is beyond the remit of NICE to recommend what is included in the Quality and Outcomes Framework.

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				- Local community-based specialty services should provide support to GPs and local physicians, should assist in local education on ME/CFS, should give guidance to them on treatments for symptoms of ME/CFS or of any future treatments for ME/CFS as the evidence emerges, and should act as facilitators for research on ME/CFS. - It currently says patients should have a review at least annually (at least 6 monthly for children) & more often if needed. Such reviews can be carried out by specialist services or in primary care. Ideally, in primary care, this review process should be incorporated within the annual Quality and Outcomes Framework (QOF), thereby incentivising GPs and primary care staff to deliver high quality care for those patients with ME/CFS on their practice lists. https://primarycare.imedpub.com/developing-quality-and-outcomes-framework-qof-indicators-and-the-concept-of-qofability.php?aid=902 https://digital.nhs.uk/data-and-information/publications/statistical/quality-and-outcomes-framework-achievement-prevalence-and-exceptions-data/2019-20	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008 - 009	017	The first bullet point the word: "fatigability" (American English) should be spelt "fatiguability" (British English) throughout the document. The third bullet point: "unrefreshing sleep" should be appended with "and/or sleep disturbance". Rationale: "Unrefreshing sleep" alone is too specific and may cause some people to dismiss the presence of that symptom when their sleep is actually disturbed in other ways and may lead to patients remaining undiagnosed. Some patients may feel better after having slept in comparison to how they feel at the end of the day – they may therefore not feel they have	Thank you for your comment. *Terms used in the guideline* After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms and hope this has added some clarity for readers. *Debilitating fatigability* has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, ' Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.

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				'unrefreshing sleep' but still have disturbed sleep. Sleep may also be unrefreshing without necessarily being disturbed.	'and sleep disturbance (or both)has been added to the third bullet point.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008 - 009	017 (Box 1 going onto pg. 9)	We are concerned that including cognitive symptoms as a required symptom for diagnosis may reduce sensitivity of the diagnostic criteria. The Institute of Medicine Criteria, International Consensus Criteria and Canadian Criteria all list cognitive dysfunction as an optional criterion (i.e., where patients must have a certain number of criteria from a list which includes cognitive dysfunction). A meta-analysis of cognitive functioning in chronic fatigue syndrome stated that one investigation, found that 89% of patients reported memory/concentration problems, while another large study memory/attention deficit problems were reported by approximately 90% of 2,073 consecutive patients. (Cockshell et al. *Cognitive functioning in chronic fatigue syndrome: a meta-analysis.* Psychol Med 2010). This fits with our experience that although cognitive dysfunction is very common, it is not present in all patients, and more so some patients do not have it initially but develop it within the first couple of years of illness. Including cognitive function as a required criterion rather than an optional criterion or common symptom list, may mean that 10% of patients will remain undiagnosed. We therefore feel that it would be better to move Cognitive dysfunction into Section 1.2.4 'symptoms may also be associated with, but are not exclusive to, ME/CFS' or to state that for diagnosis patients should either experience cognitive dysfunction or orthostatic intolerance (in line with the Institute of Medicine criteria), whilst noting that orthostatic intolerance may be present without associated changes in blood pressure or heart rate and should be assessed by presence of symptoms with changes in posture, or by measurement of cerebral blood-flow if available.	Thank you for your comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the Evidence review D-Diagnosis. The committee noted that cognitive difficulties, such as brain fog, are not a compulsory feature in the IOM, 2015 criteria but as an 'either or' criterion alongside orthostatic intolerance. Based on their experience as this being one of the most commonly reported features of ME/CFS (as you also note in your comment) the committee considered cognitive difficulties an essential criterion for suspecting ME/CFS and diagnosis and have not removed this as one of the essential criteria.

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				van Campen et al. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: a quantitative, controlled study using Doppler echography . Clinical Neurophysiology Practice. 2020; 5: 50–58. https://doi.org/10.1016/j.cnp.2020.01.003	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071 - 072	010 – 014 001 - 011	Medical education on ME/CFS has too often focussed on controversy or debate or uncertainty. When these are mentioned early on in education of a medical condition, healthcare professionals unfortunately often switch off, or assume a condition may be psychosomatic. This guideline (and especially this context section) needs to change that by stating the facts first. Yes, the remaining uncertainties and the disbelief faced are important to acknowledge, but the known facts need to be stated first to underline to healthcare professionals that there is clear evidence of biological pathophysiology, and how severely disabling this condition can be, and how prevalent it is. e.g., The context section should start with: 'ME/CFS is a complex, chronic neurological condition affecting multiple systems. It has considerable personal, social and economic consequences and a serious impact on a person's quality of life and emotional wellbeing. It is one of the most common causes of severe disability, more common than multiple sclerosis. Recent data from the UK Biobank suggests that there are over 250,000 people in England and Wales with ME/CFS, with about 2.4 times as many women affected as men.' Followed by the paragraph currently pg. 71 lines 20-25. Then followed by the paragraph currently pg. 71 lines 10-14. (If this paragraph is not moved and is kept at the beginning then it should be put in italics or smaller font) (Comment put forward by a medical professional with ME and with experience working in medical education).	Thank you for your comment. The context includes background information and is not intended to be exhaustive and sets the scene for developing the guideline. Many of things you have listed are included and commented on throughout the guideline and the discussions in the evidence reviews. To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034 - 035	021 – 030 001 - 013	Remove paragraphs 1.11.46 and 1.11.47 Rationale: there is a lack of evidence to support any claims that CBT improves overall functioning in ME/CFS (as outlined in pg. 34, line 5). Indeed, there is extensive survey evidence that more patients experience a deterioration in physical functioning following CBT, than experience an improvement in physical functioning. There is more evidence to support that it may improve psychological symptoms, as with patients who do not have ME/CFS. The risk in elaborating on CBT, even when making restrictive points about it, is that it creates the impression that CBT is somehow of particular use to ME/CFS. It is questionable to use the ME/CFS guidelines to discuss nuances of CBT while not going into similar detail in discussing other psychological therapies. Across 3 different patient surveys that asked people with ME/CFS whether or not it had helped: With regards to general health or physical health: only 6.2% - 23% stated it had helped , and 10 -26.4% deteriorated. With regards to mental health: although 41% reported improvement, 26.9% reported their mental health deteriorated following CBT. Dawes et al. (Forward ME & Oxford Brookes University). Evaluation of a survey exploring the experiences of adults and children with ME/CFS who have participated in CBT and GET interventional programmes 03 April 2019 Action for ME, Big Survey: https://www.actionforme.org.uk/uploads/images/2020/02/Big-Survey-GET-and-GET-for-people-with-ME.pdf	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). For this reason the recommendations you mention have not been removed.

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				Leary et al. ME Action UK. Your Experiences of ME Services. Oct 2019. https://www.meaction.net/wp-content/uploads/2019/10/Your-experience-of-ME-services-Survey-report-by-MEAction-UK.pdf	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	004	007 - 009	Change the bullet point with the following addition: • “can have a significant impact on people’s (and their families and carers’) quality of life, including their activities of daily living, family life, social life, emotional wellbeing, mental health, work and education” Rationale: social, financial, employment, and educational issues impact upon the physical and psychological symptoms of many chronic health conditions, including ME. This is evidenced by: https://www.kingsfund.org.uk/publications/long-term-conditions-and-mental-health	Thank you for your comment. The committee agree that all the issues you mention may be affected by ME/CFS and all addressed throughout the guideline. These are examples in this recommendation and it is not meant to be an exhaustive list.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	004	013 - 015	We are concerned that ‘ranging from being able to carry out most daily activities’ downplays the functional incapacity of the condition and is not very accurate. We have only very rarely witnessed a patient being able to carry out most daily activities and when those rare occasions have been a patient with a relapsing remitting course during a short period of remission.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. The severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee.

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					When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant. After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline and had more emphasis.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	004	005 - 006	Suggest rewording as: "Is a complex, chronic medical condition affecting multiple body systems. It is classified as a neurological condition by the WHO in ICD10. Although the details of its casual pathway remain unclear, numerous pathophysiological abnormalities have been found – including in the brain, immune system, muscle, neuroendocrine system, and abnormalities in exercise physiology which are distinct from those that are found in deconditioning" After line 6 insert: "The (Bio)psychosocial Hypothesis is not fit for purpose and should be discarded. It has played a central role in perpetuating disbelief in ME/CFS as an organic entity, and is responsible for much of the neglect, disbelief and mismanagement to which the ME/CFS patient community has been subjected over the years (as acknowledged in these guidelines). Its basic tenet was that ME/CFS does not really exist, but instead is a non-disease caused by a combination of faulty illness beliefs on the part of the patient combined with deconditioning. It totally failed to explain the exercise pathophysiology in ME/CFS patients (which is in contrast to deconditioning), the existence of multiple other symptoms in addition to fatigue, the existence of epidemics, nor the existence of the severe end of the spectrum	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to include your suggestions. Although this bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. Reference to the ICD10 classification has been included in the context section of the guideline.

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				of the illness. Neither did it explain why GET and CBT have failed to cure ME/CFS patients". Rationale: It is important healthcare professionals are aware ME/CFS is classified as a neurological disorder by the WHO classification of ME/CFS as a neurological disorder. Multiple neurological abnormalities have been identified by studies in ME/CFS, many of which are summarised in IACFS/ME. Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition, Section 3.2 Neuroendocrine abnormalities and Section 3.3 Brain abnormalities. Rationale: This has impact on patient care e.g., eligibility of patients with chronic neurological disorders for the influenza vaccine, or the risk group status in the Covid pandemic and the management implications of that. There is widespread misunderstanding about ME/CFS: A survey of trainee physicians in the northwest of England found '82% of the 44 respondents, believed ME to be at least in part psychological or psycho-somatic, with only 9% understanding that ME is a real, physical illness'. https://bit.ly/2yFAtY8 The guideline needs to clearly address and dismiss the hypothesis of ME/CFS being caused by dysfunctional illness beliefs and deconditioning, and it needs to make it clear that it is an organic disease. Not only is this needed to correct misinformation, but it is also needed to ensure that those involved in specialist teams treating ME/CFS or consulted for safeguarding cases have an up-to-date evidence-based understanding of ME/CFS i.e., that it is an organic disease and not a psychosomatic condition.	
Hope 4 ME & Fibromyalgia	Guideline	004	010 - 011	We are concerned that 'in its most severe form it can lead to substantial incapacity' downplays that level of incapacity at mild	Thank you for your comment.

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Northern Ireland				and moderate forms – even mild ME requires a 'significant reduction' to engage in activities from pre-illness levels. (or a reduction in at least 50% of functional capacity in some other criteria) which most people would term 'substantial'. ME of all severity levels was found to have worse quality of life compared to many medical conditions including multiple sclerosis and lung cancer. Lacerda et al. The Functional Status and Wellbeing of People with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome and their Carers. BMC Public Health. May 201111:402 We believe that there needs to be some mention that ME/CFS can occasionally be fatal. This is an extremely important point regarding the severity and prognosis of the disease that the majority of clinicians are unaware of. There were 88 deaths between 2001-2016 in England and Wales which were partly or fully attributable to ME/CFS (Shepherd & Chaudhury 2019)	The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	005	007 - 008	Change bullet point with the additional words: "involve family members and carers (as appropriate) in discussions and care planning if the person with ME/CFS chooses and consents to include them". Rationale and evidence: Important to acknowledge individual's right to consent to sharing of their information with others, by recognising the appropriate regional Mental Capacity Acts, e.g. - Mental Capacity Act (Northern Ireland) (2016) Acts of the Northern Ireland Assembly. https://www.legislation.gov.uk/nia/2016/18	Thank you for your comment. The committee agree that the issue of consent and choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person/child centered care is directly reinforced in the guideline sections 'approach to delivering care' and 'assessment and care planning'. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	006	001 - 006	Adding an additional bullet point at end: • Utilising alternative child-friendly, age-appropriate, communication techniques, tools and aids. Rationale: to enable understanding and communication between the child, parent, family/carer and the healthcare professional.	Thank you for your comment. Communication methods is addressed later in the information and support section of the guideline and includes the points you make.

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					In addition the committee noted that the Royal College of Paediatrics and Child Health have developed the ' Being Me' resources, with input from children and young people, to aid their communication with health professionals and have referenced these in Evidence review C-access to care to support readers of the guideline.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	006	009 - 010	We are concerned that putting emotional wellbeing first on the list of what symptoms may affect, could add to the stigma and now disproven theories of a psychological aetiology for ME. We would prefer if it could be placed later in the list.	Thank you for your comment. After considering the stakeholder comments the beginning of this recommendation has been edited to 'including activities of daily living, mobility, the ability to interact with others and care for themselves and emotional wellbeing' to match recommendation 1.1.1 describing the impact of ME/CFS.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	006	024 - 025	Change to 'Neurological symptoms such as photophobia, noise sensitivity, dizziness, ataxia, fasciculations, double vision and other visual disorders.'	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	006	026 - 027	We are concerned that only mentioning postural orthostatic tachycardia syndrome (POTS) and postural hypotension may mean that other forms of orthostatic intolerance are missed e.g. a study has now shown that even in patients with ME who did not meet the criteria or POTS or postural hypotension, they still had a significant reduction in cerebral blood flow compared to controls – most clinicians will not be aware of the possibility that ME patients may still be experiencing orthostatic intolerance without objective changes in blood pressure or heart rate. We would be keen for wording to be changed to state something to the effect of: 'orthostatic intolerance, including but not limited to POTS and postural hypotension – NB. Orthostatic intolerance may be present even without significant postural changes in heart rate or blood pressure).'	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.

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				van Campen et al. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: a quantitative, controlled study using Doppler echography . Clinical Neurophysiology Practice. 2020; 5: 50–58. https://doi.org/10.1016/j.cnp.2020.01.003	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	006	016	Add: 'intermittent paralysis' to the end of the point	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	007	001 - 016	We are extremely glad to see this included raising awareness of the realities of severe/ very severe ME and their needs	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	007	017 - 021	Very glad to see this included. Patients with severe / very severe ME often suffer with social care where there is a frequent changeover of staff – we hope this will encourage awareness amongst carer agencies or the importance of prioritising a small number of regular carers to patients with severe or very severe ME as much as this is feasible.	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	007	024 - 026	Change bullet point with the additional words: "For people with very severe ME/CFS, involve family members and carers (as appropriate) in discussions and care planning if the person with ME/CFS chooses and consents to include them". Rationale and evidence: Important to acknowledge individual's right to consent to sharing of their information with others, by recognising the appropriate regional Mental Capacity Acts, e.g. - Mental Capacity Act (Northern Ireland) (2016) Acts of the Northern Ireland Assembly. https://www.legislation.gov.uk/nia/2016/18	Thank you for your comment. 'if appropriate' has been added to the recommendation. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.

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					This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	007	002	We are concerned that the word 'choice' implies a personal preference rather than stated requirements as a result of the post-exertional exacerbation of symptoms they will endure if their requirements aren't met. Suggest rewording to 'at a level they can manage'	Thank you for your comment. Choice here indicates that it is the person with ME/CFS that makes the decision about what level of interaction is appropriate for them. For this reason your suggestion has not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	007	007	Change to 'need careful physical contact when supported with activities of daily living, taking into account possible sensitivity to touch, and heightened sensory responses to noise, light and chemicals, which may require lights to be dimmed, others to speak softly and to avoid wearing toiletries or using household products with strong smells'	Thank you for your comment. Hypersensitivity is included in the previous recommendations on symptoms people with ME/CFS may experience.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008	010 - 016	We are concerned that there is no mention of the comorbidities in which ME/CFS is more prevalent. This is vital to include, given the percentage of patients with ME/CFS undiagnosed is estimated to be 84-91% (Institute of Medicine 2015 report: Beyond Myalgic Encephalomyelitis / Chronic Fatigue Syndrome) and misdiagnosis rates as high as 68% (Johnston et al. Epidemiological characteristics of chronic fatigue syndrome/Myalgic encephalomyelitis in Australian patients. Clinical Epidemiology. 17 May 2016. 2016(8)p97-107.) Reducing undiagnosis and misdiagnosis rates are vital given that exercise is a beneficial treatment for so many other conditions (which may be a comorbidity in an undiagnosed/misdiagnosed patient or may be the misdiagnosis) but can be harmful in patients with ME. e.g., we have noticed that many patients given a diagnosis of fibromyalgia, either don't actually meet the diagnostic criteria for	Thank you for your comment. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. The discussion section of Evidence review D- Diagnosis includes a list conditions that commonly occur in people with ME/CFS and has the examples you have listed.

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				fibromyalgia but do meet the criteria for ME, or they meet the criteria for both, but their ME is not diagnosed. These patients are given physical activity advice to manage their fibromyalgia which is inappropriate for someone who also has ME and causes a deterioration in their ME. We believe the following need to be included: 1. Common comorbidities & those which a diagnosis of ME/CFS should prompt consideration of e.g. The Royal College of General Practitioners Toolkit for Ehlers Danlos Syndrome (EDS) states that a diagnosis of ME/CFS should prompt consideration of hypermobile EDS/Hypermobile Spectrum Disorder, Mast Cell Activation Syndrome and Postural Orthostatic Tachycardia Syndrome or other forms of dysautonomia) 2. Conditions which should prompt consideration of diagnosis of ME/CFS (e.g., EDS, fibromyalgia etc.) (Nb lists 1 & 2 could be combined as conditions that when diagnosed should prompt consideration of a diagnosis of ME/CFS and vice versa) 3. Conditions which ME/CFS is commonly misdiagnosed as e.g., mood disorders, medical unexplained symptoms, functional neurological disorder, fibromyalgia. With guidance on how to differentiate between them such as given in the Overview of the Canadian Consensus Document on pg. 9. (A Clinical Case Definition and Guidelines for Medical Practitioners An Overview of the Canadian Consensus Document. ISBN: 0-9739335-0-X. Pg. 9) Conditions commonly misdiagnosed as ME/CFS i.e., conditions which investigations should be undertaken to exclude (e.g., as listed in IACFS/ME. Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition,p.14-16	

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008	Prior to line 1	We are concerned that no effort at all is made in this guideline to address the fact that ME is often triggered by a viral or other infection, and the importance of identifying and treating these infections quickly. For best effect, treatment needs to be started within the first 6 weeks, yet the NHS currently neither tests for nor treats infections in suspected ME/CFS. We suggest adding the following: "Comprehensive testing to identify viral and other infections should not wait until the diagnosis of ME is confirmed after 3 months of symptoms but should be done immediately. With effective treatment, long term sequelae might be greatly reduced, or avoided altogether. Particular attention should be paid to infection aspects in the history, and these should be recorded in the patients' case notes. For example, fevers, night sweats, rashes, lymphadenopathy, joint pain and swelling. The progression of disease in relation to these symptoms should be recorded and their relationship with laboratory diagnosed infections, vaccinations, and known exposures to other persons with known infections. We would recommend that the ME Infection Screen be performed immediately upon suspicion of ME/CFS, or any presentation with significant fatigue. This should be done by the local ME/CFS service if referral to an Infectious Diseases specialist would introduce unacceptable delay. The ME Infection Screen should look for: - Enteroviruses, especially Coxsacchie B – by PCR on faeces specimen. - Herpes viruses, including Epstein Barr virus (EBV), Cytomegalovirus (CMV), Human Herpes Virus 6 (HHV-6) - by serology and quantitative PCR on blood. - Polioviruses – by PCR on relevant body fluid. - Parvovirus B19 – by serology and PCR on blood. - Adenoviruses – by serology and PCR on blood.	Thank you for your comment. The committee discussed the inclusion of trigger events when suspecting ME/CFS but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list. The context section notes that in many cases, symptoms are thought to be triggered by an infection. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.

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				- intra-cellular organisms such as Borrelia (Lyme), Chlamydia, Mycoplasma and Rickettsia (see below). The International Consensus Primer provides guidance on infection and immunological testing on page 11. These tests should be made routinely available on the NHS. http://bit.ly/IntConsPrimerME2012 Other tests to include are: - VP1 for enterovirus - antibodies to EBV dUTPase and DNApol - EBV induced gene 2 (EBI2), which is upregulated in peripheral blood mononuclear cells (PMBC). Treatments such as valacyclovir and valganciclovir should be made available to treat EBV and other herpes viruses."	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008	008	The purpose of including psychological wellbeing assessment in the components of an assessment when suspecting ME/CFS is unclear and will be misinterpreted by many healthcare professionals as meaning there is a psychological component to ME/CFS (other than the psychological impact of living with any chronic disabling medical condition). This is especially important given there has been so much misunderstanding of ME/CFS and a history of mislabelling it as a psychiatric condition or as medically unexplained symptoms. If the reason for including this here had been to assess for psychological impact of living with a chronic disabling illness, then it needs to very clearly state that (and it might be better to remove it from this section into the management section.) If the reason for including this here is to consider a mood disorder or other psychological disorder as an alternative cause for symptoms, then it needs to clearly state that, and it also needs to give clear guidance on differentiating between ME/CFS, a mood disorder, and ME/CFS with a secondary mood disorder, as patients with ME/CFS can score highly on many effects of ME/CFS can be misinterpreted as being due to a mood disorder	Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. At this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. Psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.

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				when they aren't e.g. feeling tired, not doing usual activities, withdrawing from social activities (due to their energy requirements), appetite changes, changes in appearance (due to energy involved) etc. There needs to be clear guidance that certain components of normal assessments for mood disorders such as the aforementioned cannot be relied upon in patients with ME/CFS. In addition, the response to physical activity is a very helpful point to assist healthcare professionals in differentiating between a mood disorder being the primary cause of symptoms as opposed to ME/CFS i.e., patients with ME/CFS will get worse with increased physical activity, whereas patients with mood disorders will get better with increasing physical activity. Many healthcare professionals are unaware of this, reflected in the significant rates of misdiagnosis of ME as a mood disorder and vice versa. Information included in the Canadian ME Overview would be helpful to include to guide clinicians in differentiating between ME and a mood disorder or somatoform disorder: Caruthers, van de Sande. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Clinical Case Definition and Guide Pg. 9 Differences Between ME/CFS and Psychiatric Disorders	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008	009	Given the significant rates of misdiagnosis of ME/CFS, there needs to be guidance given on what investigations should be used (both those to be routinely used and those to be considered but not used in all patients). There also needs to be guidance on differential diagnosis, and that where a differential diagnosis is confirmed, it should be considered whether it fully explains the symptoms or whether ME/CFS may be present as well. (i.e., as opposed to stating that certain differential diagnosis would exclude a diagnosis of ME, where it is possible for a patient to have both conditions) Studies looking at misdiagnosis rates:	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist

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				1. The Newcastle NHS Chronic Fatigue Syndrome Service: not all fatigue is the same - J R Coll Physicians Edinb 2010; 40:304–7 - J L Newton, H Mabillard, A Scott, A Hoad, G Spickett 2. Alternative diagnoses to Chronic Fatigue Syndrome in referrals to a specialist service: service evaluation survey - JRSM Short Rep Jan;3(1):4. Epub 2012 Jan 12. - Anoop Devasahayam , Tara Lawn, Maurice Murphy, Peter D White Investigations in the work-up for ME/CFS included in other guidelines: IACFS/ME. Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition, Section 4.3 Caruthers, van de Sande. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Clinical Case Definition and Guidelines for Medical Practitioners An Overview of the Canadian Consensus Document. ISBN: 0-9739335-0-X. Pg. 8-9	with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. In addition, the committee discuss misdiagnosis in the discussion section of Evidence review D- Diagnosis and include a list of differential diagnosis and conditions that commonly occur in people with ME/CFS.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	008	016	'specific onset' – we are concerned that although the majority of patients have an acute onset e.g., after an infective illness, there are a proportion of patients who have a gradual onset of ME and who may be missed by these diagnostic criteria. For example, Appendix 2 (Involving adults with Severe ME/CFS Symptoms…) Pg. 7 lines 41-42 state that the survey of patients with severe ME/CFS that you commissioned found that 1/3 of patients who responded had a gradual onset.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	009	017 - 023	We are very glad to see the encouragement to not delay diagnosis or advice on symptom management. We know that many patients have had delayed diagnoses and delay in receiving appropriate management advice and have suffered and had worse long-term outcomes as a result.	Thank you for your comment. Based on the qualitative evidence and their experience the committee agree it is important that people with this combination

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				This new advice will allow appropriate advice to be given even while investigations are ongoing, ensuring patients get appropriate advice earlier and are less likely to be harmed by inappropriate early self-management.	of symptoms are given advice that may prevent them getting worse as early as possible. After considering the range of stakeholder comments on the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS. In summary the edits are: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. These edits do not change the recommendations that people with suspected ME/CFS should be given advice in section 1.3.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	009	021 - 023	We are concerned that there is not enough guidance given on what alternative diagnoses should be looked into because studies have shown that a significant proportion of patients who were given a diagnosis of ME were misdiagnosed. Any list of alternative diagnoses should clarify that presence of an alternative diagnosis does not necessarily exclude a diagnosis of ME, but consideration should be given as to whether the other diagnosis fully explains the patients ME-like symptoms, or whether they may have both conditions. We have observed that many patients have undiagnosed comorbidities of conditions more prevalent in the ME/CFS patient population, and likewise many patients with these comorbidities have undiagnosed ME/CFS. We therefore believe it would be helpful to include a list of conditions which have a higher prevalence in patients with ME/CFS such as dysautonomia, hypermobile spectrum disorder	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS includes the examples you have listed.

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				and Ehlers Danlos Syndrome, fibromyalgia, mast cell activation syndrome.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	010	001 - 003	Implies not all patients will receive input from secondary care, which seems to contradict pg. 11 lines 7-8	Thank you for your comment. This recommendation refers to specialists where there is uncertainty in interpreting the signs and symptoms and the potential another condition may be the cause. The diagnosis section is clear as you say that all people should be referred to a ME/CFS specialist team for confirmation of the diagnosis and development of the care and support plan. The committee have added ME/CFS to specialist team where this is relevant to make this clearer.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	010	017 - 019	We are concerned that patients can still do too much activity whilst simply being told to 'not use more energy than they perceive they have'. The issue with post-exertional malaise is that symptoms triggered by exertion can be delayed by up to 7 days (average 24-72 hours). If patients are not also made aware of this & advised to monitor their symptoms and activities & notice if any activities are causing their symptoms to get worse 24-72 hours later, they may feel like they have enough energy to do the activity at the time and may feel like their symptom exacerbation 24-72 hours later is random. (It is not logical to assume that symptoms exacerbation could be due to activity 24-72 hours earlier being too much exertion for your current limits, when you felt fine at the time.)	Thank you for your comment. After considering the range of stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on pem and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. As you note the committee recommend a personalised approach and this

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					would include discussing with the person with suspected ME/CFS about how much rest is appropriate. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	010	020	Change “to rest as they need to” to “to rest and sleep as they need to”	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee’s decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support more detailed recommendations on rest and sleep in people with suspected ME/CFS, but they agreed the advice on rest would not be harmful in the short term before diagnosis. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this would not cause harm to anyone. Section 1.12 recommendations on rest and sleep management are for people that have been diagnosed with ME/CFS and as such are more detailed.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	011	005 - 006	Add to the sentence: “Diagnose ME/CFS in a child, young person or adult who has the symptoms in recommendation 1.2.3 that have persisted for 3 months, after excluding other possible causes for their symptoms.” Rationale: It is very important to rule out other pathologies as there is currently no diagnostic test for ME/CFS.	Thank you for your comment. This wording has been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	011	007 - 008	Change sentence to: “After diagnosis, refer adults to a Physician or General Practitioner trained in managing ME/CFS to develop a management plan. Referral to a Psychiatrist is not appropriate in	Thank you for your comment. The committee agreed this addition was not necessary as it is clear in the recommendation that people are referred to a

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				ME/CFS unless there is a psychiatric comorbidity, as ME/CFS is not a mental health issue."	ME/CFS specialist team for development of their care and support plan. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	011	013 - 014	We are concerned about the care pathway model outlined with reliance on specialist teams because: - The majority of existing specialist teams are not fit for purpose because: - Inappropriate staffing: many are led by Psychiatrists or Psychologists instead of Physicians, Paediatricians or General Practitioners. This is inappropriate as ME/CFS is a complex, multi-system, chronic medical condition. - The majority of current specialist clinics work on the theory of deconditioning and promote outdated and harmful treatments (GET and CBT). - Patients with moderate ME/CFS will struggle physically and financially to get to specialist centres unless they are local. In addition, patients with severe and very severe ME/CFS will require home visits and this is much more difficult to facilitate from a regional specialist service as opposed to a local service. - It is likely that specialist centres will struggle to meet the needs of the volume of ME/CFS patients. - Caution is required to ensure that any specialist services empower GPs and local physicians rather than disempower them. We suggest adding the following points before current point 1.5.1: 'Specialist services should be localised services and led by physicians, paediatricians and general practitioners.	Thank you for your comment. *Service design* This guideline focused on clinical care and service delivery was not included as part of the scope of the guideline and the committee are unable to make recommendations on the design of services and have not added your suggestion. *Skills* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *MDT composition* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. In addition, the committee discussed the value of naming which professionals should be in a team and as you comment no list is ever satisfactory or agreed. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care)

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				Clinics currently led by psychiatrists or psychologists or basing treatment on a theory of dysfunctional illness beliefs and deconditioning should be abolished. (Psychologists could be part of a team in specialist ME services where they provide psychological support to any patients who are struggling with living with a chronic disabling illness only). All specialist teams should include a doctor and an occupational therapist. Early occupational therapy home assessment and support is vital. Patients often also need: • district or community nurse input to enable procedures to be carried out at home, • social care, • physiotherapy, • dietetic support, • psychological support and • home visits by their doctor. All of these should be available at home should the patient require e.g., in severe and very severe ME/CFS. Every patient should have a designated case worker from the local ME/CFS service responsible for being the patients first point of contact and for co-ordinating all their health and social care needs – this should aim to reduce the exertion required by the patient by reducing phone calls and should enable a case worker to ensure the patients appointments are spaced out in a way they can manage e.g. some patients may benefit most from having appointments spaced out with weeks in-between, other patients may find it easier to have two appointments together rather than two separate trips to a clinic.'	The committee note that throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Named contact* This section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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					In addition the access to services section of the guideline recommends that the timing, length and frequency of appointment should be adapted to the person's needs. *Meeting the needs of the volume of ME/CFS patients* The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment to allow access to services. This guideline highlights areas where the specialist team should focus on (e.g. assessment. and development of a care plan) and those areas that should be done in primary care (e.g. initial diagnosis and review).
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	012	010 - 030	We believe it may be helpful to include in the management plan accessibility requirements for accessing healthcare – both outpatient and hospital stays. E.g., pg. 19 lines 17-19 says the management plan should be referred to, but there has been nothing noted here to state the management plan should include those accessibility details. E.g., we have patients who are bedbound who repeatedly struggle to get district nurse services each time their bloods need taken, and in one case being told the GP has said the district nurse can't take their bloods as they were 'too young' and 'the district nurses were only for cancer patients'. We have many patients who frequently do not access primary care services when required because the only way they can be accessed is through trying to get through on the phone for 45 minutes (potentially for more than one day in a row, as frequently by the time one gets through, the phone calls or appointments are all gone, and they are told to phone again the next day. Many patients, especially with severe ME do not have the reserve to do this and may have no one to ask to do it on their behalf (or not want to ask those caring for them when they are already having to do so much).	Thank you for your comment. A link to the section on access to care has been added to the support for activities of daily living bullet point.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	012	010 - 030	It would be helpful if the information in the personal management plan (which is updated at least annually) could be used as evidence for PIP / DLA /ESA. Many patients are reliant on these benefits and a high proportion face mandatory reconsideration and appeals which can take up 6-12 months every few years and cause a high amount of stress and relapse in the patient's ME/CFS. Having documented evidence to submit with applications vastly increases the chance of being awarded the correct points first time. However, the guidelines for the benefits state that the healthcare professionals should only use pre-existing records and previous appointments to base any evidence they provide on, and in the majority of cases healthcare professionals have never asked patients about the aspects of functioning mentioned in the descriptors in the benefit applications – patients are therefore stuck in a 'catch 22' where it is extremely difficult to get the evidence which would support their case and reduce the chances of them needing to go through mandatory reconsideration (MR) or appeal and the relapse that causes to their ME/CFS. The suggested content of the management plan will provide a record of how the patient is meeting many of the descriptors and could be further clarified to aid patients significantly in their applications at minimal extra time to healthcare professionals (and likely saving time in the long run as decreased relapses as a result of MRs and appeals is likely to lead to decreased healthcare encounters. e.g., information and support needs could specifically include reading, writing understanding speech and speaking; support for activities of daily living could be specified to include washing, dressing, meal preparation and eating; mobility aids and adaptations could be specified to include distance able to mobilise without a wheelchair etc and adapting to be in line with the benefit application descriptors e.g. can it be done as regularly as reasonably required, taking under	Thank you for your comment. NICE does not have a remit to recommend the documentation used for benefit applications.

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				2 x the length of time it would take a normal person and without triggering symptoms or causing harm.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	012	005 - 006	Change bullet point with the following additions: "current and past experiences of medicines (including tolerance, sensitivities and allergies), vitamins and mineral supplements, over the counter medications and recreational drugs."	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	012	027 - 028	We believe it would be beneficial add in here 'warning signs & triggers of flares & how to manage them'. It is currently included as part of the Therapy Blueprint plan such as would be completed by a CBT therapist. However, we believe that this is part of management of the condition for all patients with ME/CFS (i.e., not just those requesting psychological support for the effects of living with chronic illness) and that it is inappropriate placing it within a Therapy Blueprint as it is not related to psychological stress of living with a chronic illness.	Thank you for your comment. The bullet point links to the flare up and relapse section where there is further detail. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose of explaining these would be included in the blueprint.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	012	009	Glad to see access to shopping and cooking mentioned alongside dietary assessment – there are many patients with ME/CFS who struggle to access food and for whom this is not picked up by healthcare professionals. There are also many patients who meet criteria for referral to a dietitian and who would benefit from this but have missed out as it is not asked about, and the patients do not know to ask for it.	Thank you for your comment and information. The section on dietary management and strategies provides further information on dietary strategies.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	013	016 - 018	We are very glad to see this mentioned, yet aware it was also recommended in the previous guidelines yet rarely observed in practice. Are there ways to encourage awareness and compliance?	Thank you for your comment. The recommendations in the guideline reflect best practice and the committee hope the guideline will raise awareness about the optimal care for people with ME/CFS and be resource to aid implementation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	013	009 - 010	Change bullet point with the additional words: "involve family members and carers (as appropriate) in discussions and care planning if the person with ME/CFS chooses and consents to include them". Rationale and evidence:	Thank you for your comment. The committee agree that informed consent is fundamental to patient's decision making and at start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in

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				Important to acknowledge individual's right to consent to sharing of their information with others, by recognising the appropriate regional Mental Capacity Acts, e.g. - Mental Capacity Act (Northern Ireland) (2016) Acts of the Northern Ireland Assembly. https://www.legislation.gov.uk/nia/2016/18 Suggest adding in additional point: Where possible the management plan should be inputted into an ME/CFS Healthcare Passport, especially for people with severe or very severe ME/CFS. Evidence to support healthcare passports: e.g. https://www.england.nhs.uk/6cs/wp-content/uploads/sites/25/2015/03/healthcare-passport.pdf and https://www.familysupportni.gov.uk/Content/uploads/userUploads/Hospital%20Passport%20Electronic%20Form.pdf	making choices about their care and shared decision making. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding. 'As appropriate' reinforces this principle here. Documentation Types of documentation was not prioritised for review and the committee were unable to make further recommendations on documentation and have not added Patient Healthcare passports but the committee recognise the importance of people having copies of their care and support plan and have recommended this in the assessment and care support planning section of the guideline. In addition after considering stakeholder comments the management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	013	012 - 013	We are very glad to see the recognition that severe or very severe ME/CFS patients will usually require home visits. They very rarely get to see either primary care or secondary care services face-to-face due to lack of awareness of this need. They usually either go without or endure relapses for weeks after the appointment because of the exertion and level of stimuli involved in attending an appointment.	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	014	030 - 031	We are concerned that the phrasing 'may be self-managed' minimalizes the significant difference that appropriate pharmacological management where appropriate can make to some of the symptoms of ME such as orthostatic intolerance,	Thank you for your comment. *Self-management*

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				sleep disturbance and pain. (Whilst being aware that pharmacological measure will not be required in all patients with those symptoms). We have observed how many patients have had significant improvements in their quality of life when they start getting appropriate pharmacological management of the aforementioned e.g., patients who have been bedbound for decades, and when their orthostatic intolerance is finally diagnosed and treated, they are able to regain some independence in self-care, meal preparation and socialising. We are also aware how many patients avoid seeking medical advice, even when they have new symptoms requiring investigation because they assume the medical professionals will not take it seriously or will put it down to their ME without investigation. We are concerned this phrasing may exacerbate that problem. More appropriate wording may be 'Can benefit from self-management techniques' which no longer implies that self-management is the only management, and no longer implies that self-management is a treatment/cure.	*Pharmacological management* Pain relief and sleep medication were included as examples of interventions in the protocol for pharmacological interventions and orthostatic intolerance was included in the search terms for the review. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. In the committee discussion in Evidence review F- Pharmacological management the committee noted it was aware that fludrocortisone is sometimes given for orthostatic intolerance syndromes, such as postural hypotension or Postural Tachycardia Syndrome (POTS) but were not confident based on the evidence identified in the review to make any recommendations. The recommendations in managing orthostatic intolerance do include that medicine for orthostatic intolerance in people with ME/CFS should only be prescribed or overseen by a healthcare professional with expertise in orthostatic intolerance. *New symptoms* The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	015	011 - 015	We are very glad that social care is specifically mentioned. We are aware there are many patients who have been struggling and not realised they were eligible for social care because none of their healthcare professionals had asked how they were	Thank you for your comment.

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				managing with tasks such as washing, dressing, food preparation, social isolation etc, and so no one had talked them through whether social care might be available to them.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	015	004 - 007	We are very glad this is being included as we know how much patients state they benefit from being introduced to ME charity support groups and gaining a source of information, advice and a supportive community who understand. We are also aware that primary care physicians have in the past felt like they had nothing to offer patients and felt relieved when they realised there was a local support group, they could signpost patients too. We hope this will encourage awareness of local support groups so that more patients can be signposted to them earlier.	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	015	016 - 018	Add to the sentence: "Explain to people and their families and carers how to self-refer for a social care and /or carer's needs assessment from their local authority/community social care or primary care team-based social worker. Offer to make the referral for them if they prefer".	Thank you for your comment. The sub section on supporting families and carers of people with ME/CFS includes reference to the NICE guideline on supporting carers and this has more detailed information. The committee agreed that your additions did not add further clarity to the recommendation and these have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	016	012 - 015	We are concerned that there are still reports of cases of mental health act/ mental capacity act or safeguarding issues where health and social care professionals with experience in ME/CFS have been involved, but their training and beliefs of ME/CFS have not acknowledged the biological aspects and been focussed on psychosocial models and led to inappropriate sectioning in environments not appropriate to severe ME or inappropriate physical activity programmes. Can something be inserted here to ensure that those health and social care professionals with experience and training of ME/CFS actually have appropriate training and are up-to-date with research and will not make decisions which lead to harm.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. 'up-to-date' does not add any further clarity to the recommendation and for this reason your suggestion has not been added.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	016	006 - 008	Suggest rewording: 'In patients with ME/CFS, where it is felt there is indication for a safeguarding assessment, thus should be performed by health and social care professionals with training and experience in ME/CFS' Rationale: Wording needs clarified, as there is currently room to be interpreted in two ways: • All patients with ME/CFS should have a safeguarding assessment (and it should be performed by health and social care professionals with training & experience in ME/CFS). – which is currently how it has been summarised on Univadis (https://www.univadis.co.uk/viewarticle/new-nice-guidance-on-chronic-fatigue-syndrome-the-key-points-732697?s1=news) • When a safeguarding assessment is felt necessary for a patient with ME/CFS, it should be performed by health and social care professionals with training & experience in ME/CFS. (Which is what I suspect was the intention)	Thank you for your comment After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	016	009 - 011	We are very glad to see this included & awareness raised	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	017	008 - 019	We are very glad to see this included & awareness raised	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	018	001 - 012	We are very glad to see this included & awareness raised	Thank you for your comment.
Hope 4 ME & Fibromyalgia	Guideline	018	022 - 024	Add to the sentence:	Thank you for your comment. 'phone consultation has been added'.

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Northern Ireland				"This could include home visits, online consultations, video/phone consultations, written communication, and supporting their applications for aids and appliances and financial support".	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	018	015	We are concerned that the phrase 'fear of relapse' undermines the significant probability of relapse is a patient needs to push themselves in order to leave their home for an appointment. 'risk of relapse' may be a more appropriate phrase here.	Thank you for your comment. After considering the range of stakeholder comments this recommendation has been edited to 'risk that their symptoms will worsen may prevent people from leaving their home'.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	008 - 029	It would be helpful if patients with severe/very severe ME/CFS were given the same access to acute care at home services as elderly patients in their local areas where this is available. E.g., if there are services where patients require bloods with quick review of results or need IV fluids and there are services which provide these for other groups of patients in their local area, making these available to patients with severe / very severe ME could prevent relapses lasting weeks – months (and even years in some cases).	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	008 - 029	Many of these accommodations will also be beneficial to patients with moderate ME	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or hospital can be difficult. This section does make a recommendation for all people with ME/CFS and includes that any difficulties in accessing hospital care should be discussed and gives some examples of what should be considered. These are expanded on for people with severe or very severe ME/CFS taking into account there are further challenges to consider
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	001 - 007	We are very glad this is included. It is not clear who has the responsibility of discussing this with the patient e.g., is it primary care, is it the specialist team helping to write the management plan, or is it the consultant arranging inpatient care? It would be helpful to clarify whose responsibility it is, to decrease the chance of no one taking responsibility for it. If it is with primary care or the ME/CFS specialist team, it may be	Thank you for your comment. The recommendations in the guideline are directed at the health or social care professional discussing the person's needs as you note this could be one of many professionals and adding examples to the recommendations does not add any clarity for this reason your suggestion has not been added.

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				helpful to include that this should then be conveyed with emergency department staff or secondary care teams when appropriate. If it is for the consultant arranging admission, then there needs to be an awareness raising programme among them of the new guideline & these contents.	The committee note that the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan and help them access services.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	013 - 016	It may be helpful to note that patients with severe and very severe ME may require ambulance transport due to difficulties mobilising to transfer to a vehicle or because they are unable to sit up for long enough in an ordinary vehicle.	Thank you for your comment and information. This has been added to the discussion section of Evidence review C- Access to care.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	017 - 019	Add to the bullet point: "discuss the person's management plan with them (plus ME Patient Healthcare Passport where available) including information on comorbidities, intolerances and sensitivities, to plan any reasonable adjustments that are needed". Evidence to support healthcare passports: e.g. https://www.england.nhs.uk/6cs/wp-content/uploads/sites/25/2015/03/healthcare-passport.pdf and https://www.familysupportni.gov.uk/Content/uploads/userUploads/Hospital%20Passport%20Electronic%20Form.pdf	Thank you for your comment. Types of documentation was not prioritised for review and the committee were unable to make further recommendations on documentation and have not added Patient Healthcare passports but the committee recognise the importance of people having copies of their care and support plan and have recommended this in the assessment and care support planning section of the guideline. In addition after considering stakeholder comments the management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	019	029	After 'minimising strong smells' consider adding including from air fresheners or from perfumes or deodorants usually used by staff.	Thank you for your comment. These are examples of what to consider in facilitating a low stimulus environment in a hospital, it is not meant to be exhaustive and for this reason your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	020	002 - 018	We believe it would be beneficial to include these additional points in the social care assessment:	Thank you for comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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				"How they manage tasks that require going out of their home, such as shopping or taking the children to school, and whether they need help with these." "How much social contact they are getting and if they are socially isolated whether assistance would improve this" Rationale: There is a huge unmet need for support with outdoor activities of daily living, especially for single parents with ME.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	020	020 - 022	We are very happy to see this included. Receiving aids & adaptations in a timely fashion can help patients maintain independence & reduce pushing through and triggering relapses. We have observed many patients who would benefit from aids who have not had occupational therapist referral discussed by their primary care team, or who have been referred but have faced waits of up to a year or longer to get the aids or equipment. We suggest changing '(such as a wheelchair, blue badge or stairlift)' to '(such as wheelchair (Including powered and/or tilting), blue badge, commode, lifts, hospital bed and/ or hoist)'	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	020	002 - 003	Add to the sentence: "If a person with ME/CFS needs support at home, conduct social care, occupational therapy, and physiotherapy assessments, record and provide information and support on":	Thank you for your comment. This recommendation lists as a minimum the areas that should be assessed and not the specific assessments that would be done by specific healthcare professionals. Depending on the individual different assessment will be required.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	020	005	If it is possible to include 'maximum distance reliable to mobilise without a wheelchair without causing exacerbations of symptoms or taking longer than twice normal time a healthy person would take' (or whatever the up-to-date mobility descriptors are in benefit applications if they change) in this mobility section, it would serve as an extremely useful record for benefit applications – helping patients receive the correct awards and decreasing relapses triggered by mandatory reconsiderations and appeals.	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised.
Hope 4 ME & Fibromyalgia	Guideline	020	012	We suggest adding: ' text-to-speech and speech-to-text software'	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account

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Northern Ireland					that an assessment should be personalised and for this reason no other examples have been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	021	001 - 010	We suggest adding suggestions of useful adjustments to work and education, such as: "Adjustments at work or education could include home schooling, working from home, flexible or reduced hours, providing transport, designated parking space, a quieter work area with lower light settings, speech-to-text software, text-to-speech software, audiobooks, ergonomic assessment, and a place to rest when needed."	Thank you for your comment. Further information in types of adaptions and adjustments are included further in this section and in the committee discussion in evidence review A and the points your raise are highlighted there. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	021	001 - 007	We are very happy to see this included. It is unclear what lines 4-5 means: does it mean they may have periods of time off work or education before returning, or does it mean that there is a chance they may not regain enough health to return to work or education. Both are true and it is helpful to patients to be given a realistic prognosis whilst allowing room for hope. We have observed countless patients who have returned attempted to return to work when it was beyond what they could manage at that point (often encouraged to do so by well-meaning primary care so they don't 'lose confidence' and triggering relapses and deterioration sometimes lasting decades and leading to ill health retirement which may have been avoided if the patient waited longer before returning, even if that meant they lost their job and would need to look for new employment when they had recovered enough to start some work again without deteriorating their health. Given the reports of inappropriate return-to-work management in many people with ME/CFS, it would be really helpful to provide more guidance here for healthcare professionals supporting patients re: decisions about when to return to work e.g.,	Thank you for your comment and this information. The committee agree it could mean people may have periods of time off work or education before returning, or there is a chance they may not regain enough health to return to work or education. In reference to this point and the one about providing specific advice in the recommendations the committee note that any advice would be personalised and relevant to the person. The committee agreed not to add examples of organisations, as with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.

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				"Consider what types of activities they would be doing at work, the travel time to work, the social contact, the minimum hours required for a phased return and how quickly that needs to be increased. Compare that to what they are managing at the moment in terms of any similar activities, social contact, ability to travel etc. If, and only if, they are managing their activities of daily living, then gradually add in any extra activities similar to those that would be required for work, e.g., desk work, phone calls, getting up & ready for time that would be required (important as many patients are worse in the morning and can tolerate less activity in the morning). Monitor how they respond to introducing these activities and the gradual increases (only if it is not triggering PEM). If they are able to progress to managing a similar level of activity that would be required for a return to work and are managing to increase activity level at the rate that would be required for a phased return, then encourage the patient to maintaining it at home for a few weeks before attempting a return. Consideration must also be given to any treatments – e.g., if the patient is suitable for and wanting to attempt a physical activity programme or psychological therapy to support them in living with chronic illness, and if they have not yet started them, then it must be considered whether they will be able to partake in these whilst working or whether it might be better for them to undergo these therapies prior to an attempted return to work."	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	022	013 - 022	Add point between 21 and 22: mental health wellbeing. Rationale: with mental health practitioners available in some multidisciplinary primary care teams now – this service can be offered where deemed appropriate by other healthcare professionals or requested for by the patient.	Thank you for your comment. The recommendation has been edited to include,' physical, psychological, emotional and social' to reflect that people's mental health wellbeing should be considered.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	022	008 - 012	We suggest changing the order of bullet points and adding them as follows to emphasise that finding a balance within one's limits is important, as it currently could be interpreted as though they should be taking on other activities on top of training or education:	Thank you for your comment. The committee disagree that this encourages young people or children to take on other activities the second bullet point is clear it is about finding a balance and not just focusing on their education.

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				• 'They should aim to find a balance, within their energy envelope, between the time they spend on education or training, home and family life, and social activities.' • Training or education should not be the only activity they undertake • Training or education should not push the child or young person beyond their energy envelope"	Advice on energy management is in the following section on the management of ME/CFS.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	023	005 - 006	We suggest changing to: "Care for people whose ME/CFS is managed in primary care should be supported by a Physician, Paediatrician or GP led local service" Slight change to the sentence: "Care for people whose ME/CFS is managed in primary care should be supported by advice and direct clinical consultation from a local Physician, Paediatrician or GP/ANP (Advanced Nurse Practitioner) led specialist team. Such Specialist or multidisciplinary Teams, should not treat ME on a psychological or functional basis." Rationale: patients should be referred to a local consultant either at beginning to confirm diagnosis, or for ongoing review. Ideally, this should be a Consultant with a Specialist interest in ME at a local hospital. However, this may well be population size and commission service dependant, but should at least be a regionally-based service, offered locally, or on an outreach basis by virtual/remote - video/phone methods, so as not to disadvantage those unable/unfit to travel.	Thank you for your comment. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. A description of ME/CFS team has been added to the terms used in the guideline and this includes local and regional teams. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the design and delivery of services, including who leads services as this is determined locally. *Treating ME/CFS* When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. The principles of care, information and support and management of symptoms section of the guideline are clear about the approach for the care of people with ME/CFS. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be

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					difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. The committee note in the recommendations that other methods, such as online communications may be more appropriate depending on the person's symptoms. For these reasons your suggestions have not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	023	008	We agree that having a named contact whom patients can get in touch with during periods of relapse or when needing support with benefits or education or social care etc. will be very helpful. Given patients low limits for exertion, all patients should have a case worker who can help coordinate their care in order to reduce the number of phone calls or emails they need to make/write. This care coordinator should liaise with the other healthcare professionals on the specialist team, arrange their appointments and ensure the appointments are timed in a way that causes least detriment to the patient e.g., for moderate and severe patients they may need weeks between appointments to recover in-between. For patients able to travel to outpatient appointments, they may benefit from seeing multiple members of the team on the same morning/afternoon etc, for severe patients, their appointments may need to be coordinated with the time of their social care calls, and for the time of day at which the patient is least symptomatic. We suggest rewording lines 7-10 as follows: "Inform people with ME/CFS (and their family members and carers, as appropriate) of contact details for their designated case worker from their local ME/CFS service, who will help them access services and support them during periods of relapse and coordinate their appointments." We suggest rewording lines 12-15 as follows: "Inform parents and carers of children and young people with ME/CFS of contact details for their designated case worker from	Thank you for your comment and information. Lines 7-10 The committee agree and the named contact is referred to in the recommendations in the flare ups and relapse and review in primary care sections of the guideline. For this reason your suggestion has not been added to the recommendation. The wording suggestion for lines 12-15 does not add any further clarity to the recommendation, designated care worker is covered by named professional and local ME/CFS service by ME/CFS specialist team, and the recommendation has not been edited.

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				their local ME/CFS service, who they can contact with any concerns about their child's health, education or social life."	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	024	018 - 020	The majority of patients, not just children, will need help from a healthcare professional to establish what their energy limits are. The majority of patients, before given assistance with energy management, are in a 'boom and bust' pattern and will be unable to have any idea of what their energy limit is until a healthcare professional works with them to help them stabilise and monitor their activity and symptoms to work out what level of activity they can regular manage without exacerbating their symptoms. Many patients will struggle to reduce activity on good 'boom' days enough to stabilise without the support of someone experienced, because of the demands placed on them by others or life circumstances and because of the strong desire to 'do things while you can'. Overcoming this often requires support from someone experienced encouraging you that in order to have the best chance of stabilising, you need to let go of the expectations of others, learning so assertively say no, and often reduce the expectations you have of yourself.	Thank you for your comment. The committee agree it is important that people with ME/CFS are supported by a healthcare professional to develop an energy management plan.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	024	016 - 017	We are concerned that the majority of patients overestimate their limits. This is in large part because of the delayed nature of post-exertional symptom exacerbation which means that patients often feel fine during or just after over-exerting themselves. It is additionally complicated by the fact that an individual's limits can vary hour-to-hour and day-to-day: what was within their limits in the evening, may be far over their limits in the morning (natural daily fluctuation). What was within their limits two days ago may be far beyond their limits now if they exceeded their limits in the last 48 hours and are now in Post-exertional symptom exacerbation (PESE) with reduced limits (variation due to PESE). Their limits may also vary due to infection, menstruation, allergies, disrupted sleep, weather changes, exacerbations of other health conditions, or unknown factors. It is important to expand on 'fluctuating energy limit' to explain this further, to make healthcare professionals aware of this in this	Thank you for your comment. The committee agree and this is why the following bullet point includes help from a healthcare professional to recognise when they are approaching their limit (children and young people in particular may find it harder to judge their limits and can overreach them). The committee notes that the energy management plan is developed with the person with ME/CFS and a ME/CFS specialist team as part of the care and support plan and they are aware of the importance of advising people with ME/CFS on how to avoid the 'boom and bust' pattern. The fluctuating nature of the guideline is highlighted throughout the guideline and is included in the first recommendation. When writing recommendations

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				guideline so that they can in turn advise patients and families. Many patients end up with difficulties in relationships with friends and family members as they do not understand how the patient's energy limit can fluctuate so much. The majority of patients, before given advice on energy management, are in a 'boom and bust' pattern and have inaccurate gauges of their energy limit is until a healthcare professional works with them to help them stabilise and monitor their activity and symptoms to work out what level of activity they can regular manage without exacerbating their symptoms. Suggest rewording to: • "Recognises that each person has a different and fluctuating energy limit, which can fluctuate hourly to monthly. • Recognises that fluctuations in energy limit can be caused by: Post-exertional symptom exacerbation (PESE), infections, allergies, disrupted sleep, weather changes, medication changes, exacerbations of other health conditions, diurnal fluctuations and often unknown causes • Recognises that patients are usually a good judge of what they cannot do, but can sometimes overestimate what they can do within their energy limits due to the delayed nature of PESE and the frequency of fluctuations in their energy limits • Recognises that advice on the delayed nature of PESE, and training on how to monitor symptoms and activity levels to avoid 'boom and bust' patterns and create as stable a baseline as possible reduces the frequency of overestimating what is achievable within their energy limits, thereby reducing the frequency of PESE, flares and relapses	there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.

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				- Recognises that even the most diligent patients will overestimate what they can do within their energy limits at times, because of the unpredictability of fluctuations in their energy limits and the delayed nature of the onset of PESE" These points are key to energy management and will greatly assist healthcare professionals who have not yet received adequate education on the management of ME/CFS in assisting patients.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	024	004	'Be aware there is no current treatment' seems to contradict later parts of the guideline which refer to treating and managing orthostatic intolerance and other symptoms of ME. We think what was meant here was 'Be aware there is no current cure' (removing 'treatment or') There is a growing amount of experience showing that different treatments can help with aspects of ME/CFS in some patients. We believe that it is important to list them here given the burden of ME/CFS in terms of disability and quality of life. Specialists should be able to trial these treatments or advise local physicians or general practitioners to trial them. These should be mentioned here to raise awareness. E.g. cannabinoids, low dose naltrexone, pyridostigmine, melatonin, antivirals. For example: A series of three case reports compiled by people with long-term ill-health due to chronic fatigue syndrome shows the range of responses they observed when taking LDN, from life changing to a reduction in some symptoms only. (Bolton et al. *Low-dose naltrexone as a treatment for chronic fatigue syndrome.* BMJ Case Reports 2019). Information outlining more specific drug choices to treat symptoms associated with ME/CFS can be accessed via the website: https://www.uptodate.com/home The UpToDate system is an evidence-based clinical resource that includes a collection	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. *Treatments* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis. No evidence was identified that met the review protocols for low dose naltrexone and without this the committee were unable to evaluate the impact of naltrexone for people with ME/CFS.

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				of medical and patient information. It is written by over 7,100 physician authors, editors, and peer reviewers.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	024	023	Insert 'and have been stable for at least a couple of weeks' after 'improved'	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse)'.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	004 - 014	This list also needs to include orthostatic stress i.e., standing v sitting with feet down v sitting with feet up v reclining v lying flat.	Thank you for your comment. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and includes physical health. The care and support plan is the basis for the energy management plan.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	027 - 029	Activity and symptom diaries are essential for helping patients establish a baseline of activity & learning how much activity they can manage without exacerbating symptoms. This sentence makes it sound like it's an optional extra and underestimates its importance.	Thank you for your comment. In the rationale section the committee recognise there was a lack of effectiveness evidence on tools to support people to self-monitor activity management. The committee decided to recommend that activity recording should be as easy as possible, and people should take advantage of tools they are already using and gave examples of these. The committee also decided to make a recommendation for research on self-monitoring management strategies to help determine which techniques are effective.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	027 - 029	Heart rate monitoring is a key tool in energy management. It is extremely helpful in that where it otherwise takes patients 24-72 hours to observe whether activity undertaken was beyond their fluctuating limits at that time, heart-rate monitoring can provide real-time biofeedback that an individual is exceeding their energy limits. It is being used by many leading groups such as:	Thank you for your comment. In the rationale section the committee recognise there was a lack of effectiveness evidence on tools to support people to self-monitor activity management. The committee decided to recommend that activity recording should be as easy as possible, and people should take advantage of tools they are already using

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				the Workwell Foundation www.workwellfoundation.org, Prof Nancy Klimas (American researcher and physician who is the Director at the Institute for Neuro Immune Medicine at Nova Southeastern University in Miami and Ft. Lauderdale, Florida), Physios4ME https://www.physiosforme.com, Dr David Systrom (Pulmonary and Critical Care Medicine at Brigham and Women's Hospital and is the Director of the Massachusetts General Hospital Cardiopulmonary laboratory, both in Boston, Massachusetts, US. Assistant Professor at Harvard Medical School). Morning resting heart rate can also provide an indication to patients as to how their energy limits on that particular day are likely to be compared to an average day for them. It would be helpful to include more details of how heart rate monitoring can be used beneficially e.g., Davenport et al. Conceptual Model for Physical Therapist Management of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis. Physical Therapy. February 2010. DOI: 10.2522/ptj.20090047. Nb. The Workwell Foundation have made further advances in using heart-rate based pacing in the management of ME/CFS since publishing this guide 10 years ago – they have a number of more up-to-date educational resources available via their website. https://workwellfoundation.org/resources/ Additionally, the phrasing 'phone heart-rate monitor' needs clarified: there are many phone heartrate monitors which use the light and camera on the phone as an optical sensor to measure heart rate and which do not have enough accuracy for patients with ME i.e., patients with ME who are using heart-rate monitoring may need to keep their heart-rate within a 15-20 beat per minute window. Optical-based heart rate sensors (whether wrist based, or phone camera based) can be inaccurate by 30 beats per minute, therefore not providing useful bio-feedback for	and gave examples of these. The committee also decided to make a recommendation for research on self-monitoring management strategies to help determine which techniques are effective.

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				this purpose. Chest-strap or other electrical-based heart rate monitors have a higher degree of accuracy and provide useful bio-feedback for this purpose (although not all patients can tolerate them due to the higher prevalence of MCAS amongst ME patients, or pain from comorbid fibromyalgia). Many of the chest straps or electrical based heart rate monitors will sync with phone applications in which case these would be useful. Clarification is needed to ensure that monitors not providing accurate enough bio-feedback for this purpose are not recommended along-side those with enough accuracy.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	023 - 024	This needs clarified as to frequency of review which is helpful & acknowledgment that not all times at which it will be beneficial to review it can be predicted e.g., initially it will need reviewed more frequently as the patient learns the skills of energy management and interpreting how their activity is affecting their symptoms with a delay. As they become more skilled at managing & interpreting it themselves, they will need less assistance in this when they are stable. It is helpful to review the plan during relapses and during change in circumstances which may also be unexpected e.g., major life event which will take energy over period of weeks or months, changes in family demands, changes in work or education etc.	Thank you for your comment. The following recommendation is about review and includes, 'agree how often to review the person's energy management plan with them and revise it if needed.'
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	025 - 026	Very important	Thank you for your comment.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	025	018	We are very glad this is included. It needs to be expanded to convey 'Reduce activity as the first step to enable baseline of symptoms to stabilise i.e., Reduce swinging between good days and bad days).	Thank you for your comment. After considering the range of stakeholder comments this was edited to 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
Hope 4 ME & Fibromyalgia	Guideline	026	009 - 011	We are happy to see this included & agree that it is good practice, whilst also being aware that there is not current capacity	Thank you for your comment.

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Northern Ireland				for this in much of the UK. We hope this will act as a highlight of service need.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	027	005 - 006	Insert an additional bullet point between 5 and 6: "general skin integrity" Rationale: Patients bed-bound, with reduced mobility and nutritional intake are at high risk of general skin condition deterioration/breakdown – loss of skin integrity, not just at pressure points.	Thank you for your comment. Skin assessment is included in the NICE guideline on pressure ulcers referenced in the recommendation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	028	023 - 029	Studies have shown that the majority of patients with ME/CFS have some form of orthostatic intolerance, therefore some mention should be given in this section of being aware of whether the patient experiences orthostatic intolerance (which may not be apparent in postural heart rate and blood pressure changes), and if so then prioritising physical activity which is most beneficial to managing orthostatic intolerance, within the constraints of what needs to be avoided in a physical activity programme for ME e.g. prioritising recumbent exercises strengthening the core and leg muscles (but excluding the anaerobic activity parts of regimes for patients with POTS alone. e.g., Paediatric version of the Levine protocol for POTS (Paediatric version (CHOPS protocol)) can be viewed here.: https://www.dysautonomiainternational.org/pdf/CHOP_Modified_Dallas_POTS_Exercise_Program.pdf The adult version is almost identical but contains an additional 2 months prior to the start of the CHOPS programme. (The Levine protocol for adults with POTS is not publicly available but can be freely requested by a medical professional who wishes to use it with POTS patients). Similarly, many patients with ME/CFS have comorbid hypermobility spectrum disorder or Ehlers Danlos Syndrome which are also frequently undiagnosed. Screening for this and adapting exercise programmes accordingly (e.g., avoiding over-stretching, strengthening muscles around joints before starting to	Thank you for your comment. Anyone with ME/CFS that wishes to explore a physical activity or exercise programme is referred to physiotherapist in a ME/CFS specialist team, they would then assess the person. The assessment is not included in these recommendations they focus on what a programme should look like. The detail of the programme would be personalised to the person undertaking the programme. For these reasons your suggestions have not been added.

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				stretch them to avoid destabilising the joints etc) can reduce risk of musculoskeletal injury, especially where muscle conditioning has reduced due to increased physical activity for prolonged periods. e.g., The Muldowney physiotherapy protocol for EDS is outlined in his book: Living Life to the Fullest with Ehlers-Danlos Syndrome: Guide to Living a Better Quality of Life While Having EDS. 17 July 2015. Kevin Muldowney. ISBN-10 : 1478758880. Outskirts Press. Suggest adding the additional point: "Take into account any comorbidities the person with ME/CFS has and incorporate any principles of physical activity programmes which can be of benefit in those comorbid conditions, as long as they are in keeping with the energy management principles in ME/CFS. Any parts of physical activity programmes for comorbid conditions which are not in keeping with energy management principles in ME/CFS should be avoided. E.g., in patients with ME/CFS who also have Postural Orthostatic Tachycardia Syndrome (POTS), focussing on physical activity in a supine, reclined or seated position which strengthens leg and core muscles is beneficial, whereas any recommendations in POTS exercise programmes regarding cardiovascular exercise which does not follow energy management principles for ME/CFS should be avoided. Physical activity programmes for hypermobility should be assessed and incorporated in a similar way for patients with ME/CFS who have comorbid hypermobility spectrum disorder (HSD) or hypermobile Ehlers Danlos Syndrome (hEDS)"	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	028	006 - 011	Very glad to see this highlighted	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming*

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					After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS '. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	028	012 - 015	We are concerned that many patients who 'would like to incorporate physical activity into the management of their ME/CFS' many not have an informed idea of the risks of physical activity in ME and how it does not provide benefits in a similar way to other health conditions. Many patients with ME were very active prior to becoming ill. Many people are aware of how exercise benefits the vast majority of health conditions. The majority of patients are unaware of how physical activity can cause deterioration and harm in ME, and how long that harm can last i.e., decades. Many patients when first made aware of the harm it can cause, or when experiencing it themselves, assume that it will be-short lived, yet many patients are left with deteriorations lasting years to decades because of physical overexertion. In addition, Suggest rewording lines 12-15 to: "Only consider a physical activity programme for people with ME/CFS who have achieved a stable 'Only consider a physical activity programme for people with ME/CFS who are: - Managing to maintain a stable baseline of symptoms (i.e., not booming and busting) for at least a couple of weeks - Managing basic activities of daily living e.g., washing, dressing,& either managing or have someone else to manage meal preparation, grocery shopping and maintaining a clean home and clothing.	Thank you for your comment. This recommendation refers to the discussion between the person with ME/CFS and the ME/CFS specialist physiotherapist or occupational therapist about considering a personalised physical activity or exercise programme under the circumstances listed. The later recommendations in this section include further detail on how increasing physical activity should be addressed.

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				And would like to incorporate physical activity into the management of their ME/CFS."	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	028	019 - 022	Many healthcare professionals are completely unaware of this risk of physical activity programmes to ME/CFS and that exacerbations triggered by increase physical activity can last decades in some patients. This needs to be more explicitly explained in the guideline, so that healthcare professionals will be informed when telling patients about the risks and benefits, and so that the patients in turn can make an informed decision. Suggest adding to the end of line 22: "Explain that in patients where physical activity programmes make symptoms worsen, this can last from days to decades. Explain that it is important that the risk of prolonged worsening must be minimised by only engaging in a physical activity programme if they have been maintaining a stable baseline, only making any increases in activity if their symptoms have been stable at the previous level for at least two weeks, only making small increases in activity (i.e., an absolute maximum of 20% of duration or intensity), and by reducing activity and increasing rest any time their symptoms increase. Explain that the aim of a physical activity programme, is to assist the person with ME/CFS in using their energy in a way that gives them the best quality of life. Explain that although sometimes patients may be able to increase their energy envelope through a physical activity programme, that this is not achievable to all people with ME/CFS, and it is not the aim. That if the patient does experience an increase in their energy envelope, it is not expected this will be a linear process, as people with ME/CFS will often experience flares or relapses from a wide range of triggers. "	Thank you for your comment and information. This recommendation refers to a physiotherapist or occupational therapist with training and expertise in ME/CFS.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	029	017 - 022	Very glad to see this included. Suggest adding the following points: 'on the difference between low energy activities (which may include as reading or watching tv) and true rest (such as meditation, using guided relaxation, lying with their eyes shut or sleep).' 'On the importance of resting just before they become tired or symptomatic and of not pushing through due to the temptation to complete an activity as this leads to requiring a much longer recovery period and can be counterproductive'. 'Hypersomnia is common early in the illness and during flares and relapses – resisting the body's requirements for additional sleep can lead to prolonging these phases of illness and should be avoiding.' 'Some standard sleep hygiene practices, such as limiting daytime sleep, may not be appropriate in ME/CFS.' 'Consider using melatonin in patients with persistent insomnia.' 'Consider short-term trials of sedatives in patients whose insomnia persists despite other measures.' and 'Education should be provided flexibly to enable children and young people with ME/CFS to get the sleep they need.'	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	029	008 - 009	It would be beneficial to input here providing a contact for the patient to be able to get prompt access to the specialist ME/CFS physiotherapy support.	Thank you for your comment. The recommendation includes access and as part of that would be how to make contact.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	029	006	The point uses the term 'after a flare', yet it is talking about 'during and after a flare' – lines 8-11 are talking about management during a flare, therefore wording of line 6 should be adjusted to include 'during and'	Thank you for your comment. This has been edited to, 'during'.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	029	011	We suggest adding the following point: "incorporating extra periods of rest and sleep, listening to their bodies and resting or sleeping as much as they need to."	Thank you for your comment. The collaborative personalised programme includes recognising a flare-up or relapse early and outlining how to manage it, as part of this any strategies would be individual and agreed with the person with ME/CFS.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	030	013 - 016	We suggest adding the following: "Tension headaches, myalgias/arthralgias, and sensitive skin are common with CFS and can be managed symptomatically with a nonsteroidal anti-inflammatory drug (NSAID) or acetaminophen. Nonpharmacologic interventions may also be helpful. (See "Tension-type headache in adults: Acute treatment" and "Approach to the patient with myalgia" and "Approach to the management of chronic non-cancer pain in adults".) If these interventions do not work, a tricyclic agent can be initiated. When used for fibromyalgia or CFS, tricyclics do not seem to work via an antidepressant effect; when patients respond, the response is immediate (24 to 48 hours), not after a two- to three-week delay as would be expected with depression. In addition, doses much lower (10 to 20 mg at bedtime) than prescribed for depression typically are used; and in patients with coexisting mood disorders, those disorders do not seem to respond to such low-dose tricyclics." Rationale: Expansion on guidance on pharmacological management of pain in ME/CFS is helpful. Several randomized trials have shown that low-dose tricyclic therapy is beneficial in fibromyalgia (see "Initial treatment of fibromyalgia in adults"), and given the similarity in epidemiology and symptoms, some clinicians consider CFS and fibromyalgia to be part of a spectrum of disorders. However, no large trials have been conducted in patients with CFS. Accessed via the website: https://www.uptodate.com/home The UpToDate system	Thank you for your comment. *Pharmacological management* Pain relief was included as an intervention in the protocol for pharmacological interventions. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	030	004 - 006	Suggest changing to: 'Orthostatic Intolerance is extremely common in people with ME/CFS. It occurs when upright postures (e.g., standing or sitting) trigger symptoms including light-headedness, nausea, pallor, brain fog, rapid fatigue. The most common forms are	Thank you for your comment and information. The definition in the terms used in the guideline includes more information on orthostatic intolerance. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition

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				Postural Orthostatic Tachycardia Syndrome (POTS), neurally mediated hypotension (NMH) and orthostatic hypotension (OH). Patients with ME/CFS may also have orthostatic intolerance with significant reduction in cerebral blood flow without any associated changes in blood pressure or heart rate.' It is important to note that patients with ME/CFS can have orthostatic intolerance without changes in heart rate and blood pressure as demonstrated by significantly reduced cerebral blood flow in comparison to controls in a study by van Campen et al. This is clinically significance as these patients may still benefit from treatment measures such as compression hosiery and increased salt and fluid intake. van Campen et al. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: a quantitative, controlled study using Doppler echography . Clinical Neurophysiology Practice. 2020; 5: 50–58. https://doi.org/10.1016/j.cnp.2020.01.003	results in a guideline becoming unwieldy and unusable. for this reason your suggestion has not been added to the recommendation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	030	007 - 009	We are concerned that 'should only be prescribed' may cause significant delays in patients accessing treatment given that waiting lists to see a specialist in orthostatic intolerance can be 2-3 years locally. It is compounded that the fact that a number of patients will be too severe to attend a hospital outpatient appointment, and although it has been recommended that alternative formats such as home visits or remote consultations be offered in these cases, these have not been available yet, and it may be a while before services make these adaptations available. These patients would be left untreated in the draft guidelines current format. This is especially concerning given the significant impact that we have observed pharmacological treatment of orthostatic intolerance can have on patient's mobility, functioning and quality of lives once treated. E.g., one patient who had been bedbound and completely dependent on care for all activities of daily living for two decades became able	Thank you for your comment. The recommendation includes 'or overseen' indicating that it is an important there is involvement of a healthcare professional with expertise in orthostatic intolerance. This does not necessarily require referral and will depend on local arrangements. As you note the committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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				to sit up in a powered wheelchair, able to wash, dress and prepare food for herself, and to regain some social contact. We also believe that there needs to be recommendations given for non-pharmacological measures as a first step such as compression hosiery and increasing fluid and salt intake. We suggest this be reworded as follows: 'Patients with orthostatic intolerance should be offered compression hosiery (at least thigh high and at least 20-30mmHg compression) and given advice on increasing their salt and water intake as long as there are no contraindications. Pharmacological treatments for Orthostatic Intolerance should be prescribed by specialists with experience in managing Orthostatic Intolerance. If significant delay in accessing specialist input is anticipated, medications such as fludrocortisone, pyridostigmine and midodrine may be cautiously tried with advice from a clinician experienced in managing Orthostatic Intolerance. The NASA 10 Minute Lean Test may be repeated to monitor progress.'	The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	030	006 - 007	A point needs inserted here about testing for orthostatic intolerance as: 1) Many patients currently experience significant delays in the diagnosis and treatment of orthostatic intolerance due to long waiting lists for tilt-table tests (reports of delays of years), 2) a significant proportion of patients with ME/CFS report that full tilt-table tests have triggered relapses lasting months or years, and 3) a proportion of patients with ME/CFS and severe Orthostatic intolerance are too ill to undertake any form of orthostatic testing involving standing – a study has shown sitting is sufficient to reduce cerebral blood flow in severe ME/CFS – a 10-minute (or shorter) supine to sitting test may be sufficient in these patients and reduce the risk of triggering an ME relapse.	Thank you for your comment and information. In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance.

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				van Campen et al. Reductions in Cerebral Blood Flow Can Be Provoked by Sitting in Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients. Healthcare (Basel). 2020 Oct 11;8(4):E394. doi: 10.3390/healthcare8040394. We suggest a tiered screening/diagnostic approach of: A) For patients who struggle to sit with their feet on the ground: 10-minute supine to sitting test measuring blood pressure and heart rate as would be done in the NASA 10-minute lean test. This can be performed at home or in primary care and stopped earlier if patient becomes too symptomatic or meets diagnostic criteria before the 10 minutes is complete. B) For patients who can sit with their feet on the ground: NASA 10-minute lean test C) For patients who can sit with their feet on the ground, who can manage getting to an outpatient appointment without triggering prolonged post-exertional symptom exacerbation, and for whom the NASA 10-minute lean test was negative: Full tilt table test. If these patients are experiencing orthostatic intolerance symptoms, then non-pharmacological measures could be started whilst waiting for the tilt-table test appointment. We suggest the following wording: 'A full tilt table test can trigger a relapse in patients with ME/CFS. To reduce the risk of triggering a relapse and to reduce delays in diagnosis and treatment of orthostatic intolerance, a tiered screening / diagnostic process can be used: A) NASA 10 Minute Lean Test should be performed in primary care for any patient with ME/CFS who is able to tolerate sitting with their feet on the ground for longer than a few minutes	

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				without triggering post-exertional symptom exacerbation (PESE) lasting longer than a few days: http://bit.ly/BHC-10minLeanTest B) If a NASA 10 Minute Lean Test is negative, then a full tilt table test is required to exclude POTS, NMH or OH. Consideration should be given as to whether the patient is likely to tolerate this: asking the patient about how long they can usually sit or stand for without triggering PESE and whether they can attend outpatient appointments without triggering PESE. C) For patients with severe orthostatic intolerance, who are unable to sit with their feet on the ground for longer than a few minutes without triggering PESE, a supine to seated version of the NASA 10-minute Lean Test could be performed to screen for orthostatic intolerance.'	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	030	002	If CFS is the only identified cause of the sleep disturbance, pharmacologic therapies, such as over the counter products, or tricyclic agents can be tried. Clinicians experienced with CFS report that patients treated with low-dose tricyclics describe having more hours of uninterrupted sleep, although no large randomized trials have been conducted. Amitriptyline 10 mg one hour before bedtime is a good starting dose. Even though this is a very small dose, some patients still may feel groggy upon awakening; this usually passes after about a week. If this low dose does not reduce frequent nocturnal awakenings, gradual escalation of the dose is warranted. Improved sleep is usually seen within 48 hours. Accessed via the website: https://www.uptodate.com/home The UpToDate system . Additional information on the management of sleep disorders can be found in separate topic reviews. (See "Overview of the treatment of insomnia in adults" and "Approach to the patient with excessive daytime sleepiness" and "Treatment of restless legs syndrome and periodic limb movement disorder in adults" and "Nocturnal leg cramps".)	Thank you for your comment and information. Although sleep medication was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any specific recommendations for medicines or prescribing. The committee have provided general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	031	001 - 004	We would like to see here the mentioning that some patients may require pharmacological treatment of nausea. It would also be helpful to mention comorbidities which have a higher prevalence in patients with ME/CFS than in the general population and where appropriate management of those comorbidities can less the nausea and vomiting e.g. gastroparesis which is more common in patients with dysautonomia or hypermobile spectrum disorder (both of which can be present in ME) and also Mast Cell Activation Disorder – where antihistamines, montelukast, sodium cromoglycate, and H2 receptor antagonists can make a significant difference, allowing patients to eat without vomiting and re-establish a healthy weight.	Thank you for your comment. In the absence of any evidence on dietary strategies or treatments for nausea the committee made a consensus recommendation with general advice (now in the dietary management section) and expanded on this in the committee discussion in Evidence review G- Non-pharmacological management.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	032	001 - 020	We suggest adding 'Consider Mast Cell Activation Syndrome in patients with multiple food intolerances.' There have been a number of cases of patients with ME/CFS and severe food intolerances and vomiting being misdiagnosed with eating disorders but being able to regain weight once MCAS treatment has been initiated.	Thank you for your comment. Throughout the guideline the committee have recommended the importance of being aware of differential diagnoses and coexisting conditions. The committee hope that the recommendation to refer people with ME/CFS with a restrictive diet for a dietetic assessment will improve the identification and management of complications that people with ME/CFS can experience and they decided not to refer to any one particular condition noting that highlighting one condition may lead to other conditions being overlooked.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	002 - 020	Change all references to 'cognitive behavioural therapy (CBT)' or 'CBT' to 'psychological therapy' Rationale: psychological therapy offered to people with ME to date has been predominantly CBT, yet there is no evidence to suggest that this is a more appropriate psychological therapy than other varieties, and a number of large patient survey studies have shown that patients with ME/CFS have been harmed by CBT. The only reason that CBT should be specifically mentioned is to warn clinicians and patients that it is not a treatment for ME/CFS (as had been stated in the previous guidelines).	Thank you for your comment After considering the range stakeholder comments about the title not being representative of this section the committee edited the title of this section to remove psychological support recognising this only referred to CBT. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee

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				Across 3 different patient surveys that asked people with ME/CFS whether or not it had helped: With regards to general health or physical health: only 6.2% - 23% stated it had helped , and 10 -26.4% deteriorated. With regards to mental health: although 41% reported improvement, 26.9% reported their mental health deteriorated following CBT. Dawes et al. (Forward ME & Oxford Brookes University). Evaluation of a survey exploring the experiences of adults and children with ME/CFS who have participated in CBT and GET interventional programmes 03 April 2019 Action for ME, Big Survey: https://www.actionforme.org.uk/uploads/images/2020/02/Big-Survey-GET-and-GET-for-people-with-ME.pdf Leary et al. ME Action UK. Your Experiences of ME Services. Oct 2019. https://www.meaction.net/wp-content/uploads/2019/10/Your-experience-of-ME-services-Survey-report-by-MEAction-UK.pdf	agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *Treatment or cure* To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	002 - 005	Very glad to see these clarified.	Thank you for your comment.
Hope 4 ME & Fibromyalgia	Guideline	034	006 - 008	Point 1.11.44 should be reworded along the lines of: 'Psychological therapies should only be delivered by healthcare professionals who are aware of the organic pathophysiology of	Thank you for your comment. The training for health and social care professionals section of the guideline recommends that all staff that deliver care to people

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Northern Ireland				ME/CFS, of energy management principles in ME/CFS, and of the particular risks associated with overexertion (physical, cognitive or emotional) in ME/CFS.' Rationale: There is no definition (or consensus) regarding what constitutes 'appropriate training and experience' or 'expertise in CBT for ME/CFS'. The term, 'CBT for ME/CFS' is arguably a misnomer. The paragraph as it stands has no clear meaning and will likely be interpreted inconsistently. This could greatly complicate the challenge of developing a new service culture that adapts to the new guidelines i.e., that psychological therapies are not a treatment for ME/CFS but to offer psychological support for the psychological effects of living with chronic illness. It is important that healthcare professionals delivering psychological therapies to people with ME/CFS are aware that it has organic pathophysiology and are aware of the risks of overexertion (physical, cognitive or emotional) in ME/CFS given the evidence of harm caused to patients by psychological therapies. Dawes et al. (Forward ME & Oxford Brookes University). Evaluation of a survey exploring the experiences of adults and children with ME/CFS who have participated in CBT and GET interventional programmes 03 April 2019 Action for ME, Big Survey: https://www.actionforme.org.uk/uploads/images/2020/02/Big-Survey-GET-and-GET-for-people-with-ME.pdf Leary et al. ME Action UK. Your Experiences of ME Services. Oct 2019. https://www.meaction.net/wp-content/uploads/2019/10/Your-experience-of-ME-services-Survey-report-by-MEAction-UK.pdf	with ME/CFS should have training and maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. The following recommendation is clear that CBT does not assume people have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS. For these reasons your suggestion has not been added.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	009 - 011	The risks may need to be clarified in the guideline as most healthcare professionals will not be aware of the risks of CBT specific to ME/CFS (in addition most patients will not be aware that CBT could have risks) e.g., risk of deterioration if physical, cognitive or emotional energy expenditure required to engage with psychological therapy sessions is beyond the patient's energy envelope. Risk of relapse if the psychological therapy in any way encourages patients to push through symptoms or exceed their energy envelope. McPhee, G., Baldwin, A., Kindlon, T., & Hughes, B. M. (in press). Monitoring treatment harm in Myalgic encephalomyelitis/chronic fatigue syndrome: A freedom-of-information study of National Health Service specialist centres in England. *Journal of Health Psychology*. doi: 10.1177/1359105319854532	Thank you for your comment. The committee agree it is important for the risks to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that you highlight.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	003 - 004	Reword 'support them in managing their symptoms of ME/CFS; to 'to support them in managing psychological demands of chronic illness' Rationale: There is no evidence that psychological therapies assist in managing symptoms of ME/CFS. They assist with psychological distress associated with having chronic illness or with psychological symptoms from other causes. The guideline needs to clearly reflect this unambiguously.	Thank you for your comment. *CBT* The management sections of the guideline include recommendations to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any

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					recommendations for any of the interventions (see evidence reports G and H). After considering the range of stakeholder comments this recommendation has been edited to,' explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative. Offer CBT to people with ME/CFS who would like to use it to support them in managing their symptoms'. In addition recommendation 1.12.29 has been edited to clarify that CBT aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	005 - 006	Section 1.11.44 should be preceded by a new paragraph, along the lines of the following: *"Given the variety of therapies that can be considered, the choice of therapy will depend on the needs, capacities, limitations, and preferences of the individual patients themselves. In the past, many persons with ME/CFS have been given CBT, but there is no empirical basis to support a generic recommendation of CBT to universally support the psychological well-being of any patient group."* Rationale: This is required to help address the fact that psychological therapy offered to people with ME to date has been predominantly CBT, yet there is no evidence to suggest that this is a more appropriate psychological therapy than other varieties, and a number of large patient survey studies have shown that patients with ME/CFS have been harmed by CBT.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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				Across 3 different patient surveys that asked people with ME/CFS whether or not it had helped: With regards to general health or physical health: only 6.2% - 23% stated it had helped , and 10 -26.4% deteriorated. With regards to mental health: although 41% reported improvement, 26.9% reported their mental health deteriorated following CBT. Dawes et al. (Forward ME & Oxford Brookes University). Evaluation of a survey exploring the experiences of adults and children with ME/CFS who have participated in CBT and GET interventional programmes 03 April 2019 Action for ME, Big Survey: https://www.actionforme.org.uk/uploads/images/2020/02/Big-Survey-GET-and-GET-for-people-with-ME.pdf Leary et al. ME Action UK. Your Experiences of ME Services. Oct 2019. https://www.meaction.net/wp-content/uploads/2019/10/Your-experience-of-ME-services-Survey-report-by-MEAction-UK.pdf	reviews G and H for the evidence and the committee discussion on these recommendations). For these reasons you suggestion has not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	020 - 021	After Point 1.11.45 Insert a section similar to the following: 'Adjustments needed for Psychological Therapies in Patients with ME/CFS Should a person with ME/CFS seeks support from psychological therapies, the process and pace of such therapies should be adjusted to meet the person's needs and to minimise the risk of the the physical, cognitive and emotional energy involved exceeding the person's energy envelope. This might include shorter, less frequent sessions, longer-term goals and sessions delivered remotely or from home. It is important the therapist reviews at the start of each session, what impact the previous session had on the client's ME/CFS to consider if it is manageable or if the energy requirement of the sessions need reduced in some way e.g., by keeping sessions shorter, or using	Thank you for your comment. The committee agree that flexibility in accessing services and delivering care is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and cognitive difficulties may require additional time. This is addressed in the access to care section of the guideline and includes many of the points you make. A holistic personalised approach to the assessment and the management of ME/CFS is recommended throughout the guideline and the needs of the individual should be taken into account.

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				different form of communication, or by the client lying down during the session etc, or whether engaging in therapy in any way is too much for the patient at the current time. Adjustments to cancellation policy: Due to the fluctuating and unpredictable nature of the illness, people with ME/CFS will at times need to cancel sessions last minute - it is important that this does not lead to their number of sessions being reduced, as where this is the case, patients can be tempted to push through a flare to avoid losing a session, triggering a relapse. Adjustments to number of sessions offered: The number of sessions offered should be sufficient to meet the psychological needs and should take into account that it is more difficult for a person with ME/CFS to start an additional separate block of psychological therapy where the first was too short in duration to meet their needs: A therapeutic relationship takes time to establish, and this will take longer in patients with ME/CFS who can only manage shorter sessions or more spaced out sessions. Due to limited energy, a person with ME/CFS will usually require making substantial sacrifice in order to engage in any therapy session e.g., sacrificing already minimal social contact, family responsibilities, getting outdoors or even getting washed or dressed. Therefore, it is important to avoid the need for the person with ME/CFS to sacrifice further energy to build up a second therapeutic relationship, where insufficient number of sessions was given with the first . Inpatient Psychiatric Facilities: Where patients require inpatient psychiatric treatment for a psychiatric condition such as schizophrenia or suicidal risk, the principles laid out regarding access to care (sections 1.8.1-1.8.6) apply. For patients with severe ME/CFS, it should be ensured	

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				that any assistive equipment needed is available during their stay e.g., wheelchairs, hoists etc.' Rationale: Given that psychological therapies are not a treatment for ME/CFS, the main contents of a Psychological Support section in the ME/CFS guidelines should be to: ○ Emphasise how the guidelines have changed that psychological therapies should be no longer offered as a treatment for ME/CFS ○ Outline any ways in which assessment and treatment of psychological distress or psychological disorders should differ in patients with ME/CFS in comparison to the general population. i.e., 1) issues with diagnosis of psychological disorders due to symptoms which can be present in either ME/CFS and psychological disorders and 2) Adjustments needing made to management of psychological disorders or psychological distress in patients who also have ME/CFS. The normal formats of psychological therapy are often inaccessible to patients with ME/CFS due to the combined physical, cognitive and emotional energy required. Adjustments that are currently listed for patients with severe or very severe ME/CFS on pg. 35 lines 25-26 will frequently be insufficient in themselves to make psychological therapy accessible to people with severe or very severe ME/CFS, but they will be useful for people with mild and moderate ME/CFS and so should be included in a section on adjustments for psychological therapies for all people with ME/CFS. There is extensive survey evidence that people with ME/CFS have been harmed by CBT, and it is important that this section highlights adjustments that can minimise that risk e.g., sessions	

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				which can be accessed from the patients home, shorter sessions, more spaced out sessions. It is very important the therapist reviewing at the beginning of each session how the previous session affected the patient's ME, to prevent harm going unnoticed and to allow further adjustments to be made as necessary. The sacrifice that patients with ME/CFS may be making in order to engage with psychological therapies is substantial e.g., reducing already minimal social contact, being unable to engage in family responsibilities/activities they otherwise could, being unable to go outside, or even being unable to get washed and dressed on the day or for a few days after a therapy session. It is important that therapist and commissioners are aware of this and ensure that people with ME/CFS get sufficient benefit for those sacrifices. Obstacles that currently reduce that benefit are: 1) number of sessions offered being insufficient (especially important where patients with ME/CFS cannot afford the energy involved in building up a therapeutic relationship with a second therapist for a second block of therapy when they become eligible again, and 2) Not being able to make full use of the limited number of sessions they are offered because the unpredictable fluctuating nature of the illness can mean they need to cancel last minute and cancellation policies often mean that in that situation they lose that session. This also encourages patients to push through in order to not lose a session and increases the risk of going over their energy envelope and triggering a flare or relapse. People with severe ME/CFS who also have psychiatric conditions for which they have required inpatient psychiatric care e.g., schizophrenia or bipolar disorder have reported difficulties where the psychiatric wards have not had the equipment, they need to remain within their energy envelope e.g., hoists or wheelchairs.	

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	001	Change 'Psychological Support: Cognitive Behavioural Therapy' to "Psychological Support for Living with a chronic disabling Illness' Rationale: CBT should be removed from the title as psychological support does not need to be in the form of CBT – although it has been the most commonly used form to date, there is not sufficient evidence to suggest that it is more compatible with people with ME/CFS than other types of psychological therapies and there is extensive survey evidence that people with ME/CFS have been harmed by CBT. Adding the clarification of 'for living with a chronic disabling illness' to the title helps prevent any misunderstanding that psychological support is still being recommended as a treatment for ME/CFS.	Thank you for your comment. After considering the range stakeholder comments on this section the committee edited the title to remove psychological support recognising this section only referred to CBT. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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					In addition recommendation 1.12.29 has been edited to clarify that CBT aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	002	Insert 'Psychological therapy is not a treatment for ME/CFS' at the start of this point. Rationale: Given history of CBT previously being recommended as a treatment for ME/CFS, making it clear that psychological therapy is not a treatment for ME/CFS	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. For this reason your suggestion has not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	005	After 'associated with having a chronic illness', insert a new paragraph such as the following: "Healthcare professionals should take into account that, as with many physical illnesses, some symptoms of ME/CFS can overlap with those from psychological disorders (e.g., fatigue, sleep disturbance, cognitive impairment, appetite changes, palpitations.) The presence of these symptoms alone does not indicate a psychological disorder or psychological distress. Differential diagnosis is essential. Psychological assessment should therefore focus on non-somatic symptoms of psychological disorders, e.g., anhedonia, depressed mood, low self-esteem, paranoia, suicidal thoughts, or excessive worry." Rationale: There are still high rates of ME/CFS being diagnosed as psychological disorders and vice versa. Many of the symptoms	Thank you for your comment. Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses and this is included this in the assessment and planning section. CBT is included as part of the care and support plan if chosen by the person with ME/CFS.

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				usually used when screening for anxiety and depression can be features of ME/CFS without anxiety or depression being present. E.g., fatigue, cognitive impairment, sleep disturbance, nausea, palpitations etc. It is important that all healthcare professionals assessing for and treating psychological stress or disorders in patients with ME/CFS are aware of this.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	005	Make the last sentence a new point and reword: Never offer psychological therapies including CBT as a treatment or cure for ME/CFS. Always advise patients that psychological therapies, such as CBT, cannot be used to treat ME/CFS.' Rationale: Given the history of using CBT as a treatment for ME/CFS, and due to the ample evidence around the world to show that some clinical practitioners can be slow to adapt to revised regulatory guidelines, especially where they hold high levels of allegiance to a preferred therapy, the point that psychological therapies should not be offered as a treatment for ME/CFS needs strengthened. It is important to minimise risk of patients, families and healthcare professionals believing psychological therapies can treat ME/CFS and of psychological therapies being incorrectly offered as a treatment for ME/CFS. Scott, T., Mannion, R., Davies, H.T.O., & Marshall, M.N. (2003). Implementing culture change in health care: Theory and practice. *International Journal for Quality in Health Care*, *15*, 111-118. Jackson, V. E., & Muckerman, A. (2012). Navigating regulatory change: Preliminary lessons learned during the healthcare provider transition to ICD-10-CM/PCS. *Perspectives in Health Information Management*, *9*, 1d. Grol, R., & Wensing, M. (2020). Effective implementation of change in healthcare. In M. Wensing, R. Grol, & J. Grimshaw (Eds), *Improving Patient Care: The Implementation of Change in Health Care*, 3rd edition. Hoboken: Wiley.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	034	014	Remove 'improve functioning and'. Rationale: there is a history of parents and families facing inappropriate child protection proceedings because they would not pursue CBT or Graded Exercise Therapy for their children as they were concerned that it could make them worse. It is essential that this guideline makes it extremely clear that psychological therapies are only expected to assist with any psychological distress associated with living with a chronic illness and are not expected to improve functioning or help manage ME symptoms. It is also essential that the guideline makes it clear that psychological therapies in patients with ME may cause harm, especially due to the cognitive and emotional energy requirements, and that any decision to embark on psychological therapy should weigh up the expected benefits and risks to the patient's ME/CFS and their mental health. The guideline must expand on what those risks can be as the majority of healthcare professionals are unaware. McPhee, G., Baldwin, A., Kindlon, T., & Hughes, B. M. (in press). Monitoring treatment harm in Myalgic encephalomyelitis/chronic fatigue syndrome: A freedom-of-information study of National Health Service specialist centres in England. *Journal of Health Psychology*. doi: 10.1177/1359105319854532 Across 3 different patient surveys that asked people with ME/CFS whether or not it had helped: With regards to general health or physical health: only 6.2% - 23% stated it had helped , and 10 -26.4% deteriorated With regards to mental health: although 41% reported improvement, 26.9% reported their mental health deteriorated following CBT. Dawes et al. (Forward ME & Oxford Brookes University). Evaluation of a survey exploring the experiences of adults and children with ME/CFS who have participated in CBT and GET interventional programmes 03 April 2019	Thank you for your comment and information. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the range of range of stakeholder comments this bullet point has been edited to,' aims to improve their quality of life, including functioning'. Noting the overall aim is improve quality of life. The committee agree that the risks and benefits should be discussed. This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks for the person and able to ensure the person with ME/CFS makes an informed choice.

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				Action for ME, Big Survey: https://www.actionforme.org.uk/uploads/images/2020/02/Big-Survey-GET-and-GET-for-people-with-ME.pdf Leary et al. ME Action UK. Your Experiences of ME Services. Oct 2019. https://www.meaction.net/wp-content/uploads/2019/10/Your-experience-of-ME-services-Survey-report-by-MEAction-UK.pdf	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	035	001 - 011	The components listed in pg. 35 lines 1-2 and 5-11 should be part of the review and management plan of people with ME/CFS, it should not be part of psychological therapy. We are concerned that a psychological therapist is not best placed to refine self-management strategies for sleep activity and rest: this should be done with a healthcare professional who is experienced in physical healthcare management. Where this is done with a CBT therapist, it runs the risk that given the majority of those who have experience in CBT in ME/CFS were previously using it with the aim of addressing "dysfunctional illness beliefs" and "deconditioning causing by fear-avoidance behaviour", if they become involved on advising patients on sleep, activity and rest then they run the risk of causing harm by encouraging patients to push through symptoms and increase activity in fixed increments as they had been doing previously.	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	035	023 - 026	Suggest amending paragraph as follows: 'There has been an unmet need in the provision of psychological support to people who have severe and very severe ME/CFS, as the physical, cognitive and emotional energy demands of psychological therapies are often above their energy envelope and can trigger flares and relapses. Treatment plans should conform to all ethical and clinical standards relevant to the use of psychological therapies with people who have severe physical illness. The individual should be consulted to identify their physical, cognitive and sensorimotor limitations, what adjustments may make psychological therapy accessible to them, what they can manage	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or focusing for periods of time can be difficult, and particularly so for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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				without causing their ME to deteriorate. , Treatment approaches should take into account of the balance of ME/CFS and psychological wellbeing. Every effort should be made to make adjustments that provide a form of psychological support that is accessible to the individual. Therapies would need to be delivered at home or remotely. Sessions may need to be as short as 5-10 minutes. Some therapies which may be more accessible include: • Therapy which can be delivered by email correspondence, audio messages, or live text chat. • Creative therapies which allow the expression of emotions whilst reducing the cognitive demands of putting them into words. • Resources which can be accessed in the persons own time and pace – whilst not a replacement for one-on-one therapy, this may offer some support if one-on-one therapy is beyond the person's ability at that time. Other adjustments which may help include: • reducing environmental stimuli during the psychological therapy session e.g., darkened room, therapist using a quiet voice. • reducing physical and orthostatic demands during the session e.g., the patient may find it easier lying down or using speakerphone, headphones or a laptop rather than holding a phone. ' Rationale: There is no evidence to suggest that CBT should be mentioned above any other psychological therapies. The adjustments listed in in lines 25-26 should be listed as recommendations for all patients with ME/CFS. For the majority of patients with severe or very severe ME/CFS, these	Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS.

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				adjustments will still be insufficient to make it achievable within their energy envelope. As a result, there has been a substantial unmet need of the psychological needs of patients with ME/CFS. Clear examples of adjustments which may help make psychological support accessible to those with severe ME/CFS. To support this submission to the consultation process, two different online support groups of patients with severe ME in the UK were consulted to establish whether they had been able to access psychological support with the adjustments listed in lines 25-26, whether it had been beneficial, and whether they had experienced any other adjustments or formats of psychological therapy and whether these had been successful. A number of people with severe ME/CFS expressed that even with the adjustments listed, the physical, cognitive and emotional energy demands of therapy were more than they could manage without their ME deteriorating. One patient mentioned that although it caused her ME to deteriorate after each session, the benefits to her mental health outweighed this. Of those who had accessed psychological therapy while having severe ME/CFS, a number mentioned the things they had to sacrifice in order to manage the psychological therapy sessions e.g., contact with family or friends (including those they live with), being able to get to the garden for fresh air, or being able to get washed or dressed that day and a couple of days afterwards. One patient with severe ME/CFS mentioned they had found web-based therapy helpful which consisted of either therapy via email or live text chat communication that was available on demand at a time that suited them. A number of other people with ME/CFS stated that this was the format they felt most likely to be able to manage within their energy limits. One patient with severe ME/CFS stated they had found remote psychotherapy helpful with the sessions being limited to 5-10	

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				minutes at the start & only being able to manage them if lying down and not having to hold a phone. A number of different psychological therapies were mentioned by individuals with severe ME/CFS as having helped psychological stress from living with chronic illness, including: Acceptance Commitment Therapy, Dialectic Behavioural Therapy, Somatic Experiencing therapy, and art therapy.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	035	018 - 019	Before the section 'Additional Principles of care for children and young people with ME/CFS', Insert a new section similar to the following: 'Changes to Previous recommendation regarding CBT in ME/CFS. Previously CBT was recommended as a treatment for ME/CFS under the now no longer accepted hypothesis that 'dysfunctional illness beliefs' were a causative or maintaining factor in ME/CFS. Although the causal pathway of ME/CFS is still unclear, the organic pathophysiology of ME/CFS is clearly evident. There is some qualitative evidence that CBT can cause harm in patients with ME/CFS. Further, there is no empirical evidence to suggest that CBT is any more suited than other psychological therapies to supporting patients with ME/CFS in coping with the psychological distress associated with living with a chronic illness. Where treatment conventions change, there is a challenge to change service culture and risk that some clinical practitioners will be slow to adapt to revised regulatory guidelines, especially where they hold high levels of allegiance to a preferred therapy. The risk of existing services which have provided psychological support not adapting to the change in the evidence and guidance needs addressed. Clinical audits should therefore be regularly preformed of services offering psychological support to patients with ME/CFS and should cover: theoretical basis for treatment offered (whether it is offered as a treatment for ME/CFS or to	Thank you for your comment. This guideline will replace CG53 and it is not necessary to comment in the recommendations on the changes and would be confusing. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				support living with chronic illness), adjustments provided to make psychological support accessible to patients with ME/CFS (including those with severe and very severe ME/CFS) and impact of treatment on physical and mental health (including capturing of any harm caused). Rationale: Given the particular history of ME treatment conventions in the UK, including those now no longer supported by NICE, extreme care must be taken regarding the use of CBT with persons who have ME/CFS, particularly in services that have a long history of providing CBT. There is ample evidence around the world to show that some clinical practitioners can be slow to adapt to revised regulatory guidelines, especially where they hold high levels of allegiance to a preferred therapy. The new NICE treatment guidelines should explicitly refer to this known challenge of changing service culture. They should openly acknowledge the difficulty some services will experience in instituting new treatment approaches. This risk, and the need to address it, should be explicitly set out in the subsection on CBT (paragraphs 1.11.43 to 1.11.45). Scott, T., Mannion, R., Davies, H.T.O., & Marshall, M.N. (2003). Implementing culture change in health care: Theory and practice. *International Journal for Quality in Health Care*, *15*, 111-118. Jackson, V. E., & Muckerman, A. (2012). Navigating regulatory change: Preliminary lessons learned during the healthcare provider transition to ICD-10-CM/PCS. *Perspectives in Health Information Management*, *9*, 1d. Grol, R., & Wensing, M. (2020). Effective implementation of change in healthcare. In M. Wensing, R. Grol, & J. Grimshaw (Eds), *Improving Patient Care: The Implementation of Change in Health Care*, 3rd edition. Hoboken: Wiley.	

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	035	017	Guideline needs to be more explicit about potential risks of CBT as the majority of healthcare professionals will be unaware of them. McPhee, G., Baldwin, A., Kindlon, T., & Hughes, B. M. (in press). Monitoring treatment harm in Myalgic encephalomyelitis/chronic fatigue syndrome: A freedom-of-information study of National Health Service specialist centres in England. *Journal of Health Psychology*. doi: 10.1177/1359105319854532	Thank you for your comment. The committee agree it is important for the risks and benefits to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that you highlight and be able to support the child or young person and their parents or carers to make an informed choice. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	036	001 - 021	Many ME experts recommend that patients with ME/CFS should not receive live vaccines due to immune system dysregulation often found in ME. We believe this should be mentioned somewhere in the guideline and could be included in the Managing Coexisting Conditions section.	Thank you for your comment. The administration of vaccines for people with ME/CFS was not prioritised by stakeholders during the development of the scope or by the committee when finalising the evidence review questions. As such evidence on vaccines has not been searched

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					for or reviewed and the committee were unable to make any recommendations on this topic.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	036	005 - 006	We believe that there should be an additional point after this which highlights conditions which have a higher prevalence in patients with ME/CFS. We believe this is important as we have observed patients often have these comorbidities undiagnosed or may have one of these comorbidities with undiagnosed ME/CFS. e.g., could state: "A number of conditions have a higher prevalence in patients with ME/CFS. Many of these comorbidities are underdiagnosed, as is ME/CFS. Therefore, a diagnosis of ME/CFS should prompt consideration of whether these comorbidities are present, and likewise a diagnosis of one of these comorbidities should prompt consideration of whether ME/CFS may be present. Common comorbidities which should be considered include: Fibromyalgia Ehlers Danlos Syndrome and Hypermobile Spectrum Disorder Mast Cell Activation Syndrome Postural Orthostatic Tachycardia Syndrome and other forms of dysautonomia Sleep apnoea (central and obstructive) Multiple chemical sensitivities" For reference please see: IACFS/ME. Chronic Fatigue Syndrome Myalgic Encephalomyelitis Primer for Clinical Practitioners 2014 Edition, Section 4.6 Co-existing Medical Conditions Caruthers, van de Sande. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Clinical Case Definition and Guidelines for Medical Practitioners An Overview of the Canadian Consensus Document. ISBN: 0-9739335-0-X. Pg. 3.	Thank you for your comment. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not infer any importance of the condition in reference to co-existing with ME/CFS.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	036	007	The following points should be inserted: "Where indicated, refer people with ME/CFS to other specialists who are able to help manage associated conditions, such as Postural Orthostatic Tachycardia Syndrome (POTS), Fibromyalgia, Mast Cell Activation Syndrome, etc. Where people with ME/CFS need to access secondary care for other specialties, considerations in section 1.8 should be provided for as needed, and funded (e.g., doctor to visit patient at home). The number of trips to clinic or hospital should be minimised, for example by co-ordinating investigations to be done at the same visit. Patients with severe and very severe ME/CFS who require investigations may need admission as they may be unable to manage being transported and the investigations on the same day."	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. See the access to care section of the guideline.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	037	005	After '-to-day variation' suggest adding 'and a reduction in level of functioning or energy envelope'	Thank you for your comment. 'and a reduction in level of functioning or energy envelope' is implied with a sustained exacerbation of symptoms and does not add any further clarity to the recommendation and for this reason has not been added.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	037	009	Suggest adding 'to a level consistent with the reduced energy envelope during the flare and increasing periods of rest or sleep' – Rationale: Patients can reduce their activity levels but still be tempted to do more activity than is within their reduced energy envelope (as they find it hard to accept the level of reduction of activity required). However, this leads to further PESE and can often lead to a flare progressing into a relapse.	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies and levels of activity would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	038	006 - 009	This seems to be inconsistent with Pg. 37 line 18 – pg. 38 line 5: which suggests that the person should be contacting a named contact & having a review each time they have a relapse. Perhaps it is meant to mean that the for the first couple of relapses should contact a named contact with expertise in ME (in primary or secondary care) and have a review as outlined in 1.13.4 and 1.13.5. During these reviews the potential triggers and management strategies for relapses will be incorporates into the patients' management plan. On subsequent relapses, the patient can attempt self-management using their management plan in the first instance, and if they need assistance or if their relapse is persistent or if they are unable to identify the cause of the relapse then they could contact their named contact for review? (We believe it is important to include that being unable to identify the cause should prompt the patient to contact their named contact as we have observed that often when bloods are done on patients with a relapse of unknown trigger, something is picked up such as a deficiency or an infection). Whether it is meant that patients should be reviewed during every relapse or during any relapse for which they would like assistance, then this should be added to pg. 39 lined 6-7 (section 1.14.2).	Thank you for your comment. This section has been reordered and in summary, strategies to manage flare ups and relapses should be included in the care and support plan, if a flare up and relapse cannot be managed then the person should contact their named contact for support, in particular for a relapse (if a review is needed) there are some examples of factors to consider. The committee hopes this adds clarity to this section.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	038	008 - 009	Change to: "advise the person to contact their named contact in the primary care team or case worker from their local ME/CFS service for review."	Thank you for your comment. **This has been edited throughout the guideline to ME/CFS specialist team.**
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	039	013 - 014	It would benefit patients enormously if discussion of what can and cannot be achieved could include the descriptors used for PIP/ESA. This would assist as a record of evidence for patients, reducing frequency of mandatory considerations and appeals which are a common source of stress triggering relapses.	Thank you for your comment. The recommendations in the review section of the guideline include the minimum areas for assessment and documentation for all people with ME/CFS. This is not intended to be an exhaustive list and should be tailored according to the individual. These areas can be used as the basis for a discussion on accessing disability support where appropriate.

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					The committee noted in Evidence review J: Review of Care that written assessments, and reassessments, are important for accessing disability support and a scheduled review is such an opportunity.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	039	018 - 019	Insert additional bullet point between 18 and 19: "mental health wellbeing".	Thank you for your comment. 'Psychological' has been added to emotional and social wellbeing.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	039	009	Change 'discharge letter' to 'letters' (the patient may still be under the specialist ME/CFS team.)	Thank you for your comment. After considering the stakeholder comments this recommendation has been edited to 'clinical communications from the ME/CFS specialist team, including (if relevant) discharge letter' to be broader.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	039	021	Change 'named contact' to 'case worker' The patients named contact should specifically be a case worker who can coordinate their case between the members of the multidisciplinary team to reduce the number of phone calls the patient needs to make (and frequently struggle to manage) and to coordinate the timing of their appointments to reduce the risk of flare or relapses being triggered by appointments e.g. by how appointments are spaced out, or timing the appointments to the patients best time of day as much as possible, especially in patients with severe and very severe ME/CFS.	Thank you for your comment. 'Named contact' links to recommendation 1.10.3 in the section on multidisciplinary care. This recommendation clarifies that it is the named contact that coordinates care and supports access to services. The committee agreed this term is well known and did not change 'named contact' to case worker.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	040	017 - 021	We are very glad to see the need for training to be evidence-based, created with input from patients and includes monitoring and competency frameworks.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	040	011 - 012	There has been such a paucity of medical, nursing and allied health professional (AHP) education on ME at undergraduate and postgraduate levels and where it has been covered it has often been covered in the context of psychological conditions or medically unexplained symptoms and functional neurology. We therefore believe that it is crucial that the guideline highlights that medical, nursing and AHP education on ME should be included on the undergraduate medical, nursing and AHP curriculums, and in postgraduate general practice, advanced nursing practice (ANP), AHP, paediatric and medical curriculums (including general medicine, emergency medicine, neurology and rheumatology). We also believe it is crucial that the guideline clarifies that ME /CFS should be taught as a complex, multisystem, chronical medical illness and not as a psychological condition or as medically unexplained symptoms or functional neurology. We believe the following points should be inserted: 'ME/CFS should be included in the undergraduate medical, nursing and AHP curriculums, and postgraduate Physician, Paediatric, General Practice, Advanced Nurse Practitioner (ANP) and Allied Healthcare Professional (AHP) curriculums. All doctors and healthcare professionals should understand that ME/CFS is a complex, multi-system, chronic medical illness, not a psychiatric condition or a functional neurological disorder. It is classified by the WHO and SNOMED-CT as a neurological disorder. All Physicians, Paediatricians, General Practitioners and ANPs must be competent diagnosing and managing ME/CFS.' 'Medical, nursing and AHP education should begin immediately, given the current poor state of knowledge and attitudes. Medical, Nursing and AHP Schools must incorporate ME/CFS into the curriculum by the next intake in September 2021, and all doctors, nurses and AHPs graduating from July 2022 onwards must:	Thank you for your comment. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula.

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				• Understand that ME/CFS is a complex, multi-system, chronic medical illness, not a psychological or psychiatric condition. • Know the most common symptoms of ME/CFS (debilitating fatigue, post-exertional symptom exacerbation, sleep disturbance, cognitive difficulties, orthostatic intolerance, pain). • Know who to ask for help if they suspect ME/CFS (General Practitioner, ANP, Physician, Paediatrician specialising in ME/CFS). • Know that Graded Exercise Therapy and CBT based on the deconditioning theory is harmful in ME/CFS, and that any exercise or physical activity programme requires great caution. ' 'Health Education England, its equivalents in devolved nations and medical, nursing and AHP Royal Colleges must incorporate ME/CFS into the postgraduate Physician, Paediatric, General Practice and Advanced Nurse Practitioner curriculums immediately, with the following initial learning objectives (to be updated as scientific knowledge on ME/CFS grows): • Be able to diagnose ME/CFS. • Be able to exclude other alternative diagnoses as appropriate. • Understand the biological nature of ME/CFS – that it is not a psychological or psychiatric condition. • Understand the long-term nature of ME/CFS, the level of disability it can cause, and its impact on patients and their families. • Know the common symptoms of ME/CFS and commonly associated conditions. • Be willing to take a patient-centred approach to management.	

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				• Know that Graded Exercise Therapy and CBT based on the deconditioning theory is harmful in ME/CFS and reject their use as treatments for ME/CFS.' Rationale: The need for medical, nursing and AHP education and a shift in attitudes is urgent and educational resources are ready to be rolled out with institutional support.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	040	017 - 018	Training programmes must be developed by the correct people in order to reflect the more accurate updated scientific understanding of the illness and not outdated 'dysfunctional illness beliefs and deconditioning' models. We suggest changing the wording to: "provide evidence-based content developed by and in collaboration with: • Practicing ME Physicians and Paediatricians, General Practitioners, ANPs and AHPs with a special interest in ME/CFS who take a biomedical approach towards ME/CFS. • Medical, nursing and allied health professionals who have ME/CFS, especially those who also have expertise in Medical, nursing or AHP education. • ME/CFS patient organisations. "	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	040	001	Change the heading 1.147 to: "When deciding on how often and where or by what method reviews or reassessments might be needed and conducted for children and young people with ME/CFS, take into account:"	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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					When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As this point is made elsewhere your suggestion has not been added to the recommendation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	040	010 onwards	Insert additional subsection to 1.14 Review: "People with severe or very severe ME/CFS People with severe or very severe ME/CFS should be reviewed in their homes as getting to clinic will cause a significant flare or relapse." Add an additional bullet point - risks/benefits to the patient's symptoms/condition of choice of location and method of review/reassessment e.g., home visits or virtual consultations by video/phone. Rationale: patients with severe/very severe ME/CFS, or those with a 'flare' may not be able to leave their homes for a consultation or may find face-to-face too stressful. Offering alternative methods such as home visits or video/phone reviews/assessments offers increased choice.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	041	009 - 011	In patients with orthostatic intolerance, postural position is another type of activity that needs considered in an energy management plan e.g., patients may only be able to manage sitting with their feet on the ground for minutes at a time (or in very severe cases, not at all). The longer they have their feet on the ground, the less cognitive or social or physical activity they may be able to manage & vice versa. Patients may or may not be aware of this themselves, so it will be helpful to discuss it with them. Where patients are able to have their feet on the ground for a short amount of time in a day, then splitting the duration they can tolerate into regular shorter time periods, to reduce the duration of time periods spent recumbent (e.g., interspersing time spent with feet raised with 30-120 seconds sitting with feet on the	Thank you for your comment and information. After the considering the stakeholder comments the committee added, 'different activities combine and interact to cause a cumulative impact for the individual.' to recognise that the impact of each activities is not separate.

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				ground) can help reduce any worsening effects of long periods of recumbent postures on orthostatic intolerance. It should also be noted that in patients with ME, physical, cognitive or social over exertion can cause orthostatic intolerance to worsen – something which is not observed in patients with orthostatic intolerance who do not have ME.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	041	005	We believe the guidelines should include a section on audit of services given that care or patients with ME/CFS has been largely inadequate to date and given the significant changes in the guidelines. We suggest the following wording: "The performance of ME/CFS services must be audited. Data such as these must be collected annually: • Time between initial presentation and diagnosis. • Length of symptoms before patients present. • Whether patients are managed by a formal community-based ME/CFS service, existing generic local services, a Psychiatrist or Psychologist led specialist clinic, or a Physician/Paediatrician/GP led specialist clinic. • Whether patients have a designated case worker and who this is (OT, other AHP, social worker, ME nurse, etc.) • Severity category – mild, moderate, severe, very severe. • Severity category in the previous year and at initial presentation/diagnosis. • Time between diagnosis and first OT assessment. Whether this was done at home. • Whether patients received their regular review (annually for adults, 6 monthly for children). If not, why not. • Whether patients are in employment, education or training. Full time or part time.	Thank you for your comment. The committee agree that audit is an important part of measuring performance in services but this guideline focused on clinical recommendations, the development of audit systems was not included as an area in the scope and the committee are unable to make recommendations in this area. Your comments will also be considered by NICE where relevant support activity is being planned.

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				• Were patients or their families the subject of Safeguarding investigations. The outcome of the investigations. The effect on the patients' health. • Sample of patients' views of the services. ○ – Diagnostic process for ME/CFS including timeliness. ○ – Are their health care needs being met, what needs to change? ○ – Are their social care needs being met, what needs to change? ○ – Are health services accessible, e.g., blood tests, patient transport, scans, appointments? ○ – Are social services accessible, any barriers to access? ○ – Do they feel supported and understood? If not, which part of the service is falling short?"	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	042	014 - 015	"fatigability" (American English) should be spelt "fatiguability" (British English).	Thank you for your comment. The term fatigability has now been replaced with fatigue
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	042	006	We suggest adding: 'This can fluctuate day-to—day and hour-to-hour. It is reduced further during a flare or relapse.'	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	043	015 - 016	Change 'all activities of daily living' to 'many or all activities of daily living'.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the

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					definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	043	021 - 022	We suggest changing 'when upright, usually when standing, but it can also occur when sitting' to 'when in more upright postures. The posture changes required to trigger orthostatic intolerance will vary according to severity e.g., in patients with mild orthostatic intolerance it may occur only on standing, in patients with severe orthostatic intolerance it can occur from any position which isn't completely flat i.e., includes reclining in bed.' Rationale: We believe the current wording significantly underestimates how disabling orthostatic can be as it hugely overestimates the level of orthostatic stress required to trigger symptoms, i.e. in some patients it can be triggered by any position which is not completely flat – this has huge implication on access to treatment as for some patients even the movement required for ambulance transfer while staying relined will trigger orthostatic intolerance, and for many patients the amount of time that they can be seated with their feet on the ground rather than raised is limited which causes access issues with transport to access appointments unless it is by ambulance on a stretcher. van Campen et al. Reductions in Cerebral Blood Flow Can Be Provoked by Sitting in Severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients. Healthcare (Basel). 2020 Oct 11;8(4):E394. doi: 10.3390/healthcare8040394.	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as lightheadedness, near-fainting or fainting, impaired concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	043	001	We suggest wording needs altered to indicate that average duration of a flare will vary from patient to patient and most likely varies in accordance with illness severity. Rationale: We asked members: "What duration cut-off would you use to distinguish between:	Thank you for your comment.

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				• a shorter transient worsening of symptoms (e.g., a 'flare') • and a longer-term exacerbation of symptoms (which may lead to longer term reduction in your energy envelope) (e.g., a 'relapse')" We gave options of 3 days, 7 days, 14 days and 21 days. 24 members (people with ME) voted: 19 selected 14 days, only 4 selected 3 days, 4 selected 21 days, and 1 selected 7 days. Whilst it is a small sample, this indicates that the definition given of 3 days is unlikely to apply to many patients with ME, and that the cut-off point for the average length of a flare vs a relapse varies from patient-to-patient.	The reference to 1-3 days has been removed and 'after a few days' included.' A relapse lasts longer than a flare up' has been added to this definition. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	043	021	Remove 'blood pressure and'. Studies have shown that patients with ME can have orthostatic intolerance resulting from significant drops in cerebral blood flow which are not always accompanied by changed in blood pressure or heart rate. van Campen et al. Cerebral blood flow is reduced in ME/CFS during head-up tilt testing even in the absence of hypotension or tachycardia: a quantitative, controlled study using Doppler echography . Clinical Neurophysiology Practice. 2020; 5: 50–58. https://doi.org/10.1016/j.cnp.2020.01.003	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as lightheadedness, near-fainting or fainting, impaired concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	044	018 - 020	Orthostatic stress should be added to the list of types of exertion which can trigger Post-Exertional Symptom Exacerbation / Post-Exertional Malaise. See Institute of Medicine report, Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness (2015), http://nap.edu/19012, Pg. 106, table 7.1, major symptoms column. This fits with our reports from	Thank you for your comment. The examples in the definition are not meant to be exhaustive and for this reason your suggestion has not been added.

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				patients of their experience that PESE can be triggered by orthostatic stress alone.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	044	001 - 002	Suggested change of wording to ensure this definition is inclusive of patients with severe and very severe ME/CFS: 'categorised into activities of daily living, mobilising, occupational, sports, conditioning, household, or other activities' Rationale: The current wording excludes patients with severe ME/CFS whose physical activity will not fall into any of those categories. For people with severe ME/CFS, physical activity will fall into categories of movement required for washing, dressing and toileting, movement required for eating and drinking, mobilising (usually within the home and that will be too much for many) and stretching.	Thank you for your comment. The definition does include that, physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen. The committee agree that the impact would vary in individuals with ME/CFS and agreed to leave the definition broad.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	044	020	Change '12 to 48 hours' to '12 to 72 hours'. Studies have found that the delay can be from less than 1 hour to 7+ days with up to 72 hours being the most common time-period. Holtzman et al. Assessment of Post-Exertional Malaise (PEM) in Patients with Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS): A Patient-Driven Survey. *Diagnostics* 2019, *9*, 26; doi:10.3390/diagnostics9010026. We feel it is important to add here a clarification that the worsening of symptoms can last months to decades where the overexertion has been at a level significant enough to trigger a relapse. This is important as clinicians need to be aware of how prolonged the effects can be in order to inform patients and so that informed decisions can be made e.g., re: returning to work, physical activity programmes etc. This information enables the patient and clinician to understand the importance of making any increases in activity very gradual, monitoring for delayed PEM, and avoiding a level of exertion which is triggering PEM or leading to fluctuations.	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.
Hope 4 ME & Fibromyalgia	Guideline	044	028	We believe that 'similar to illness onset' should be changed to 'similar or worse than at illness onset'.	Thank you for your comment. The person's symptoms and level of disability may be like illness onset." has been deleted.

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Northern Ireland				Rationale: many patients deteriorate to levels of functioning worse than they experienced at illness onset. This is especially true for patients with very severe ME, or the upper end of severe ME.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	045	001 - 007	We suggest rewording lines 2-7 as: "People with severe ME/CFS are predominantly housebound and/or bedbound. They are often unable to leave the house or have a severe and prolonged after-effect if they do so. They may depend on a wheelchair for mobility and may have severe cognitive difficulties. They are often extremely sensitive to light and noise. They often require assistance with activities of daily living such as washing, dressing and food preparation. " Rationale: We strongly believe that the definition of severe ME/CFS currently included is too restrictive and will miss many patients who are otherwise defined as having severe ME, and who would require the adaptations for severe and very severe ME/CFS outlined elsewhere in the draft. Specifically, ''unable to do any activity for themselves or can carry out minimal daily tasks only (such as face washing or cleaning teeth)' and 'severe cognitive difficulties' are too restrictive. There are many patients who do meet the criteria of being predominantly housebound or bedbound, who will usually have a severe and prolonged after-effect if they do leave the house, but who may only have mild or zero cognitive impairment most of the time (but may have periods where the cognitive impairment becomes moderate – severe when in a symptoms flare). In addition, some of these patients can carry out activities more substantial than those listed, for example light crafts, wash themselves weekly or fortnightly or preparing meals with adaptations such as using slow cookers and pre-prepped ingredients.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.

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				If the current definition of severe and very severe ME /CFS in the guideline is used, then these patients will be excluded even though they are unable to leave the house without severe and prolonged after-effect. As a result, healthcare professionals may not offer these patients the accommodations suggested for patients with severe ME, or consider the points suggested for severe ME for these patients. In addition, stating that patients with severe ME/CFS 'have severe cognitive difficulties' is likely to create obstacles for those patients with severe ME/CFS who do not have severe cognitive difficulties and who occasionally drive short distances on good days to appointments which cannot be facilitated from home etc.	
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	045	011 - 016	We believe that including consideration of 'warning signs', triggers of flares and management strategies for triggers within a therapy blueprint for CBT, a psychological therapy, confuses the issue that ME /CFS is not a psychological condition. We believe that considering 'warning signs', triggers of flares and management strategies is useful for all patients with ME/CFS and should be facilitated by a non-psychological therapist e.g., by a GP, a medical doctor, an occupational therapist, an advanced nurse practitioner or a physiotherapist.	Thank you for your comment. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose of explaining these would be included in the blueprint. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	065	014	We suggest the following be inserted after line 14: "Whilst recognising the limited extent of evidence which exists for the management of pain in patients with ME/CFS, the beneficial effects to individuals of the medications mentioned has value and is worthy of recommendation. See: Guideline Principles of care for people with ME/CFS - Managing pain pg. 30 lines 13-16." (Recommendations for pharmacological management of pain taken from Up-to-date were given in a comment 93, pg. 30, lines 13-16)	Thank you for your comment. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. This has been added to the rationale section for managing pain. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	010 - 014	Suggest using term Myalgic Encephalopathy (given issues with name Chronic Fatigue Syndrome & if decision remains that there is not enough evidence of brain inflammation to use the term Myalgic Encephalomyelitis.)	Thank you for your comment. The committee agrees there is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	015 - 019	The first & second sentences should be switched in order. The majority of introductions to medical conditions will include what the condition is before discussing its prevalence.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	017 - 019	'Considerable' isn't specific enough and could easily underestimate the impact ME/CFS has. Numerous studies have shown that it's quality of life impact is greater than multiple sclerosis or many types of active cancer. As a comparison, the NICE guideline for Multiple Sclerosis states 'It is the commonest cause of serious physical disability in adults of working age.'	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	027 - 028	Suggest altering to 'It lasts longer, often life-long…' Rationale: Stating it lasts longer than simple-post-illness fatigue leaves room to grossly underestimate the chronicity of ME/CFS.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.

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Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	011	Suggest adding in, 'Although research has shown a number of abnormalities in the brain in ME/CFS, ' before 'there is little pathological evidence…'. Reasoning: Many healthcare professionals are unaware of the abnormalities found in the body in ME/CFS in research, including in the brain. Given the stigma and misunderstanding surrounding ME/CFS, some healthcare professionals may misinterpret a lack of evidence around brain inflammation as a lack of any brain abnormalities.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	071	017	Strongly suggest changing 'multisystem' to 'neurological' in line with WHO classification of ME/CFS as a neurological disease. This has important impacts on patient access e.g., to the flu vaccine, or ,in the recent pandemic, to whether or not they are listed as vulnerable or how they will be prioritised when a vaccine is being issued. New wording could be 'It is a complex, chronic neurological condition affecting multiple systems.'	Thank you for your comment. This has not been edited but the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to this section.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	072	014 - 016	This sentence needs to make it clear that there are significant reports of harm. Terms like 'controversial' or 'uncertainty about their effectiveness' simply convey a lack of certainty over their efficacy and do not convey the potential for harm – it is important this is acknowledged so that healthcare professionals are informed themselves in order that they can inform patients of risks and benefits.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Hope 4 ME & Fibromyalgia Northern Ireland	Guideline	072	014	The rest of the guideline has acknowledged that CBT & GET are not 'treatments' for ME/CFS. Therefore, the word 'treatment' needs removed here & replaced with a more appropriate term such as 'management strategies'	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. In the context you mention the use of treatment does apply.
Institute of Osteopathy	Guideline	026		In section 1.11.8 you do suggest "Refer people with ME/CFS to a specialist ME/CFS physiotherapy or occupational therapy service" but don't mention osteopathy here.	Thank you for your comment. No evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence

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					reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
Institute of Osteopathy	Guideline	026		In section 1.11.11 you continue by suggesting "Include physical maintenance in the management plan for people with 18 ME/CFS. Think about including the following: • joint mobility • muscle flexibility • postural and positional support • muscle strength and endurance • bone health • cardiovascular health." Osteopaths are trained for 4-years at undergraduate level, are regulated by statute and were awarded Allied Health Professional status by NHS England in 2017. They are qualified to provide all of the above support and it is not clear why they have been excluded from this section. The NICE lower back pain guidelines (prior to 2016) did suggest that manual therapy (as conducted by an osteopath, chiropractor or physiotherapist with appropriate training) should be offered for lower back pain. However, in 2016 this was changed to "Consider manual therapy (spinal manipulation, mobilisation or soft tissue techniques such as massage) for managing low back pain…" and the individual professions were removed from the guidelines as it was seen to be the technique that was relevant, not the profession that administrated it. This is in direct contradiction to the ME guidelines that does specifically mention professions. This lack of consistency should be addressed. There is a section that refers to osteopathy under the complimentary/alternative section. We are now considered to be AHPs, so we feel that it is inappropriate to refer to osteopaths as complimentary/alternative therapies.	Thank you for your comment. No evidence was identified to support recommending treatments and osteopathy services for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy. Osteopathy is described by the NHS website as an example of complementary and alternative treatments https://www.nhs.uk/conditions/complementary-and-alternative-medicine/.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Institute of Osteopathy	Guideline	027		The main concern is that in section 1.11.16 you specifically state "Do not offer - therapies derived from osteopathy" and you do not say the same for chiropractic or other therapies so it would appear inappropriate to single out osteopathy, and this reference to osteopathy we feel should be removed.	Thank you for your comment. After considering the stakeholder comments the committee agreed to remove the reference to osteopathy.
ME Action UK	Equality Impact Assessment	001	Question 3.1	The Equality Impact Assessment states that "the groups identified in the equalities impact assessment during scoping were considered through the development of the guideline, however there was no or limited evidence identified for these groups and it was agreed no separate recommendations for these groups were to be made". (These groups are listed as: Older people; Pregnant women; Black and Minority Ethnic people; and Men, as well as those from low socioeconomic backgrounds and those living in rural settings. *Equality Impact Assessment questions 1 & 2*.) In light of this concerning lack of evidence, we recommend adding a research recommendation considering access to care and outcomes for people with ME in groups with potential equality issues.	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
ME Action UK	Equality Impact Assessment	001	Question 3.1	We suggest that there is evidence that black and minority ethnic people have specific issues relating to accessing information and support (e.g. Evidence Review C p17 and p22 and from feedback from our community) and would like to see this impact	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage.

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				acknowledged in the Assessment. We have also noted this in our comments on the Guideline on p15 line 6.	When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
ME Action UK	Equality Impact Assessment	001	Question 3.2	The committee did not cite any additional potential equality issues to those identified during the scoping process. We are concerned that in its discussions the committee does not appear to have acknowledged one of the most obvious inequalities, which may be impacting access to healthcare for a large proportion of people with ME/CFS. The Guideline should recognise that substantively more women than men are thought to have ME/CFS, possibly by as much as a ratio of 4:1.[1] Evidence indicates that women are often not taken seriously when reporting their symptoms and the severity of those symptoms, and that women's symptoms are frequently psychologised.[2,3,4,5] This is particularly concerning in relation to ME because the disease has a history of being put down to	Thank you for your comment. The prevalence of ME/CFS in different populations was not identified as a priority area by stakeholders in the scoping of the guideline and was not included in the scope. As such an evidence review was not carried out and the committee are unable to make a recommendation on this topic. The committee note that sex is a protected characteristic in the 2010 Equality Act.

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				"unhelpful illness beliefs" and "avoidance of activities",[6] for which patients have been referred to cognitive behavioural therapy as a treatment or cure for ME (an approach the committee now rejects in the draft Guideline). We urge the committee to acknowledge that the disproportionate prevalence of ME in women; the difficulties faced by women in having their symptoms taken seriously; and that these may create gender-based inequalities that should be recognised in the Guideline in order to help healthcare professionals provide tailored and equitable healthcare services. We suggest that the Guideline recommends that healthcare professionals should "Be aware that ME is more common in women than men and the negative impacts of gender-based assumptions." 1. ME/CFS in women and men, ME Research UK, (2015) https://www.meresearch.org.uk/sex-differences-in-mecfs/ 2. Mirin, A. A. (2020). Gender Disparity in the Funding of Diseases by the US National Institutes of Health. *Journal of Women's Health*. doi: 10.1089/jwh.2020.8682. 3. Chen, E. H., Shofer, F. S., Dean, A. J., Hollander, J. E., Baxt, W. G., Robey, J. L., ... & Mills, A. M. (2008). Gender disparity in analgesic treatment of emergency department patients with acute abdominal pain. *Academic Emergency Medicine*, *15*(5), 414-418. https://pubmed.ncbi.nlm.nih.gov/18439195/ 4. Hamberg, K. (2008). Gender bias in medicine. *Women's Health*, *4*(3), 237-243. doi:10.2217/17455057.4.3.237 5. Hoffmann, D. E., & Tarzian, A. J. (2001). The girl who cried pain: a bias against women in the treatment of pain. *The Journal of Law, Medicine & Ethics*, *28*, 13-27. http://dx.doi.org/10.2139/ssrn.383803;	

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				6. Burgess, M,. Chalder, T. (2004) PACE Manual for therapists - Cognitive behavioural therapy. https://me-pedia.org/images/b/b4/PACE-cbt-therapist-manual.pdf	
ME Action UK	Equality Impact Assessment	002	Question 3.4	We welcome the committee making specific recommendations in relation to severe and very severe ME, including the recognition that some of these recommendations may require additional resources.	Thank you for your comment.
ME Action UK	Equality Impact Assessment	002	Question 3.5	The answer here is incorrect. The committee has acknowledged that physical activity can have an adverse effect on people with ME. The recommendation of physical activity programmes, with the included proviso that for some people with ME this can worsen their symptoms due to their illness, is the definition of a recommendation leading to an adverse impact due to the person's disability. The answer can only be no if the committee removes the recommendation for physical activity programmes and replaces it with access to safer advice around physical activity that is not premised upon incremental increases.	Thank you for your comment. As detailed in the EIA the guideline has recommended the option of physical activity and exercise management for people with ME/CFS but only in specific circumstances and when developed and supervised by a specialist physiotherapist in ME/CFS. There are recommendations on energy management that address all activity. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies).

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ME Action UK	Equality Impact Assessment	002	Question 3.6	We very much welcome the committee's identification of children and young people with ME, and people with severe or very severe ME, as groups for special consideration requiring separate recommendations.	Thank you for your comment.
ME Action UK	Evidence Review A	006	023	Evidence Review A looks at the evidence on information and support for people with ME. On page 6 line 23, it states "No evidence was identified for social care professionals caring for people with ME/CFS." This major gap should surely warrant a research recommendation.	Thank you for your comment. This line has been deleted social care professionals were included in the protocol in evidence review B. Evidence review A does identify the social care needs of people with ME/CFS and these are discussed in the committee's discussion and interpretation of the evidence.
ME Action UK	Evidence Review G	326	020	"The committee agreed that CBT has a role in helping to manage the psychological effects of a chronic illness such as ME/CFS and can be particularly helpful for improving 'secondary disability' such as sleep, depression, and dietary issues" We question why sleep has been included here under 'secondary disability' when unrefreshing sleep is a core symptom of ME. We recommend you remove sleep from this list.	Thank you for your comment. This has been edited to, 'symptoms associated with ME/CFS'.
ME Action UK	Evidence Review H	098	General	The formatting has gone wrong here - we can't read part of the effectiveness evidence on the PDF version.	Thank you for alerting to this.
ME Action UK	Guideline	General	General	Overall, this Guideline is a significant improvement on the 2007 Guideline, and we would like to thank the committee members, and especially the lay members, for their extensive and hard work over the past couple of years. We are thrilled to see acknowledgement of the stigma people with ME have faced; the additional recommendations for people with severe or very severe ME and for children and young people; the recommendations on different ways to access care (such as phone, video conference or home visits); the recommendation to provide aids and adaptations without delay and also the acknowledgement that cognitive behavioural therapy is neither a treatment nor a cure for ME.	Thank you for your comment. *Training* **The committee agree that the training section of the guideline is important to the delivery of the care. They discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops (see evidence review B).** The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline.

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				In particular, we'd like to congratulate the committee on their recognition that graded exercise therapy has caused significant harm, and their decision to recommend against this therapy in the draft Guideline. This particular change is a triumph of evidence based decision making that puts patient safety first, in the face of significant pressure from those with vested interests. We wish to convey the deep relief people with ME felt upon hearing this news, as Ben H, person with ME, wrote on twitter: "You'll never see so many patients so pleased and emotional about having no treatment for their illness. That's how unscientific, ineffective and harmful GET has been. No treatment is better than a harmful one." All of us at #MEAction UK urge you to stand by this decision. While this draft Guideline is a major improvement, there is a need for clarification on some issues, and we remain concerned that certain recommendations could allow harmful practices to continue. We therefore argue for: ● Clarity around who will be providing care, and an explicit recommendation for a physician, preferably a consultant, to be part of every specialist team. ● Strengthening and expanding the section on training, to ensure the paradigm shift this Guideline lays out works its way into practice. ● Proactive follow up from a physician for those with suspected ME ● Moving recommendations on safeguarding into the section on principles of care, as the stand-alone safeguarding section has already been misused. ● The removal of the section on physical activity programmes, with access to specialist advice on physical activity instead being offered under the section on energy management.	To note the training recommendations have been edited. . *Biomedical research* Biomedical research was not included in the scope of this guideline as a topic to consider, and therefore we are unable to make research recommendations on this topic.

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				● Further downgrading of CBT, with broader guidance on the principles of any psychological support for people with ME and training required for any healthcare professional providing this. ● The removal of language around goals and incremental increases in activity - stabilisation is key and the energy management approach already enables increases in activity where the person has improved. ● A clear message from NICE that ambitious biomedical research is required	
ME Action UK	Guideline	General	General	We continue to oppose using the term chronic fatigue syndrome (CFS), and considering this committee is at present recommending new terminology such as PESE, energy envelope, energy management and more, we strongly urge them to make a recommendation that this disease is called myalgic encephalomyelitis (ME), with a note that it has formerly been known as CFS. As committee members have recognised, people with ME have faced significant stigma. The term CFS has contributed to this. We strongly urge the committee to take an active stance on this issue, instead of passively accepting an outdated misnomer.	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning. • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
ME Action UK	Guideline	029 - 033	017 - General	We recommend this section be edited to include more details on symptoms and symptom management. We understand the reasons why the recommendation is that there is no overall treatment for ME, but in our experience specific symptomatic treatment can significantly improve our quality of life. It would be helpful for GPs to be given a clearer steer as to what can be offered, rather than assuming relevant knowledge. Suitable prescriptions might include amitriptyline for pain and reverse	Thank you for your comment. After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily

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				body clock; betahistine for nausea and dizziness, antihistamine based sleeping tablets, etc. It would be helpful for patients and GPs to be given a list of suitable examples like this.	living or would like to incorporate a physical activity or exercise into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS.
ME Action UK	Guideline	001	009 - box	"This Guideline will update NICE Guideline CG53 (published August 2007)." We have been assured by various NICE employees since 2017 that this new Guideline will replace CG53, not just update it. Please ensure this is clearly stated on the final Guideline.	Thank you for your comment. This has been edited to, 'this Guideline will update and replace NICE Guideline CG53 (published August 2007)'.

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ME Action UK	Guideline	002	001	Whilst we acknowledge that this Guideline should not be used for those simply experiencing fatigue post-COVID 19, there is clear evidence from previous viral outbreaks that a significant minority will go on to develop ME.[1,2,3] This box must make clear that having had COVID-19 does not exclude a patient from an ME diagnosis if they meet the criteria, and where a patient does meet the criteria, advice from this Guideline on exercise and energy management in particular should override other advice. Suggested addition: "However if a person does meet the criteria for suspecting or diagnosing ME/CFS after COVID-19, then this Guideline should be used, advice on energy management should be given, and investigations to exclude other conditions should continue." 1. Moldofsky, H., & Patcai, J. (2011). Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC neurology*, *11*(1), 37. 2. Hickie, I., Davenport, T., Wakefield, D., Vollmer-Conna, U., Cameron, B., Vernon, S. D., ... & Lloyd, A. (2006). Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. *Bmj*, *333*(7568), 575. Garcia, M. N., Hause, A. M., Walker, C. M., Orange, J. S., Hasbun, R., & Murray, K. O. (2014). Evaluation of prolonged fatigue post–West Nile virus infection and association of fatigue with elevated antiviral and proinflammatory cytokines. *Viral immunology*, *27*(7), 327-333.	Thank you for your comment. At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations. NICE are developing and updating the COVID-19 rapid guidelines in order to reflect that evidence.
ME Action UK	Guideline	004	004	Add an additional bullet point here stating that ME can "affect any age group". As the supporting documentation on children and young peoples finds, there is still significant stigma and disbelief that is unique to	Thank you for your comment. A sentence noting that ME/CFS can affect all ages has been added to the context section. Children and young people have been highlighted in the guideline and it is clear they can be affected by ME/CFS.

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				this group, it is therefore vital that all professionals begin with an understanding that ME can affect any age group.	
ME Action UK	Guideline	004	005	Agree.	Thank you for your comment.
ME Action UK	Guideline	004	007	We suggest that this is changed from "can have a significant impact on people's quality of life" to "has a substantial impact on people's quality of life". We agree the impact on quality of life is very important to get across, and are pleased to see this sentence. Recommendation 1.2.3 p8 line 14 states that ME should only be suspected if "the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels", we believe it more accurate to state here that ME "has substantial" impact, instead of adding in the qualifier of "can have". This change of wording is backed up by evidence that the quality of life for people with ME is lower than for many other debilitating illnesses.[1] Falk Hvidberg, M., Brinth, L. S., Olesen, A. V., Petersen, K. D., & Ehlers, L. (2015). The health-related quality of life for patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *PloS one*, *10*(7), e0132421).	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
ME Action UK	Guideline	004	016	We strongly agree with this statement and the two bullet points below. It is vitally important that health professionals recognise this and actively work to remedy it. We especially appreciate the acknowledgement that people with ME may be hesitant to involve health and social care professionals because of the stigma they have faced. We thank the committee for including this.	Thank you for your comment.
ME Action UK	Guideline	005	003	The wording "Health and social care professionals should: "acknowledge to the person the reality of living with ME/CFS" does not go far enough. Both those who assume the illness is	Thank you for your comment. The first recommendation in this section clarifies that, 'ME/CFS

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				psychological and those who are aware of the science demonstrating biological dysfunction can readily acknowledge "the reality". We suggest "acknowledge to the person the reality of living with ME and that, while not fully understood, research demonstrates pathophysiological abnormalities".	• is a complex, chronic medical condition affecting multiple body systems and its pathophysiology is unclear'. For this reason your suggestion has not been added.
ME Action UK	Guideline	005	005	Add "or rebuild" to this bullet point, so that it reads "take time to build or rebuild supportive, trusting and empathetic relationships" From the two community calls we held about the Guideline, we received strong feedback that many people who have been ill for a long period of time now have almost no contact with health professionals. As the stigma people with ME experience, acknowledged in 1.1.2, has driven some people away from the healthcare system, it should be noted that relationships may need to be rebuilt, not simply built.	Thank you for your comment. The recommendation is clear that health and social care professionals should build trust, this includes rebuilding trust.
ME Action UK	Guideline	005	007	We very strongly support this recommendation. Many people with ME have told us stories of how their partners, parents or carers were excluded from appointments despite the person asking them to be present. We note that a young person quoted in the evidence you commissioned also tells of this experience referencing interactions which did not consider the impact on the participant. This included a need for family support as ME3 states in Supporting Documentation Appendix 1 p16 line 6: "my mum wasn't allowed to come in with me... it was quite scary, it was the first time I'd ever been into a medical appointment without my mum". Thank you for including this recommendation.	Thank you for your comment.
ME Action UK	Guideline	005	010	We strongly support this recommendation for early and accurate diagnosis.	Thank you for your comment.

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ME Action UK	Guideline	005	012	We strongly support this recommendation, but raise concerns later in our response about who will carry out this monitoring and review.	Thank you for your comment.
ME Action UK	Guideline	005	018	As various parts of the management plan that are laid out in recommendation 1.5.2 could not be described as an intervention, we propose changing the word intervention to "aspect" in this sentence.	Thank you for your comment. The management and management of symptoms sections of the guideline set out the strategies and treatments to support people with ME/CFS with managing their symptoms. Intervention has been replaced with treatment to match the rationale and impact section for these recommendations.
ME Action UK	Guideline	005	020	We strongly agree with this recommendation, including specifying "family, friends, health and social care professionals and teachers."	Thank you for your comment.
ME Action UK	Guideline	006	007	Under awareness of severe or very severe ME, add a further bullet point that ensures health professionals are aware a small minority of those with very severe ME die. Suggested language: "Be aware that very severe ME can lead to death in a minority." Deaths from ME are rare, and ME is rarely recorded on death certificates. Better understanding of ME as a serious disease and reporting of deaths would give more accurate figures. In England and Wales, between 2001 and 2016, 88 death certificates stated that the death was either partly or fully caused by myalgic encephalomyelitis/chronic fatigue syndrome,[1] which is less than six deaths per year. Mentions of postviral fatigue syndrome (benign myalgic encephalomyelitis), deaths registered in England and Wales, 2001 to 2016. (2018) ONS	Thank you for your comment. This recommendation raises awareness about the symptoms that people with ME/CFS may experience and supports the following recommendation on what this means for how people live. A bullet point on mortality is not relevant to this recommendation.
ME Action UK	Guideline	006	008	While we welcome the recognition of the range of debilitating symptoms that affect people with severe and very severe ME, in the feedback we received as we wrote this response, many people with moderate or even mild ME noted that they too experienced some or many of these symptoms.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe

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				Be aware that people with severe or very severe ME may experience some of the following symptoms more severely and these can significantly affect their emotional wellbeing, communication, mobility and ability to interact with others and care for themselves:	ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
ME Action UK	Guideline	006	008	In the feedback we've received, and in evidence [redacted][1] people with severe or very severe ME report experiencing episodes of paralysis. Add paralysis to this list. Crowhurst, G., & Crowhurst, L. (2013) Paralysis, a qualitative study of people with Severe Myalgic Encephalomyelitis http://carersfight.blogspot.com/2013/08/paralysis-qualitative-study-of-people.html	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Action UK	Guideline	006	022	In the feedback we have received while writing this response, a few people requested the addition of diarrhoea to this list.	Thank you for your comments. The examples included in this section are based on the committee's knowledge and experience of people with severe and very severe ME/CFS and are the examples are not meant to be an exhaustive list.
ME Action UK	Guideline	006	028	This section, including the bullet points, is excellent and a vital inclusion in the Guideline.	Thank you for your comment.
ME Action UK	Guideline	007	008	Consider expanding this bullet point to read:	Thank you for your comment.

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				"need aids such as electric or manual wheelchairs, noise protection and dark glasses or eye masks"	After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Action UK	Guideline	007	017	We strongly support this recommendation - having different professionals doing personal care can significantly exacerbate symptoms of people with ME. Awareness of the person's needs and consistency is very important.	Thank you for your comment.
ME Action UK	Guideline	007	022	We strongly agree with this recommendation, and believe it could significantly help people with severe or very severe ME to access the care they need in the safest way possible.	Thank you for your comment.
ME Action UK	Guideline	008	001	We are pleased to see a section on suspecting ME and not just diagnosis, with recognition that early advice on symptom management can be critical. As Evidence Review D p53 line 5 states: "Early diagnosis is seen as critical to better care and may also improve prognosis. Appropriate advice on activity and rest given in the early stages of ME/CFS is seen as the key to prevent deterioration (see Evidence review E: pre diagnosis strategies)." We support the committee's decision to include a section on Suspecting ME/CFS.	Thank you for your comment.
ME Action UK	Guideline	008	002	We agree with this recommendation. We are pleased that the committee has not said this is a diagnosis of exclusion.	Thank you for your comment.
ME Action UK	Guideline	008	006	We agree that a comprehensive clinical history should be taken	Thank you for your comment.

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ME Action UK	Guideline	008	007	We agree that a physical examination should be carried out.	Thank you for your comment.
ME Action UK	Guideline	008	008	This recommendation is unclear as to what exactly a psychological wellbeing assessment is, nor is this obvious from the evidence reviews or any rationale given as to why this is part of initial assessment. However Evidence Review C p20 line 29 states "Patients also expressed the opinion that their doctors ignored their physical symptoms and focussed more on the depressive symptoms, reporting that their more physical symptoms were disregarded in favour of any that could be described as pertaining to depression or to mental health issues." During our community call that discussed this issue, multiple attendees raised concerns that standardised depression questionnaires, such as the PHQ-9, could lead to misdiagnosis due to questions about energy levels, trouble concentrating and troubled sleep. While it is important that people with depression get appropriate treatment and care, the issues around misattribution of symptoms should also be mentioned. We recommend you clarify what a psychological wellbeing assessment should include, and how misattribution of symptoms can be mitigated.	Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. At this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions. Psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
ME Action UK	Guideline	008	009	What does the word 'baseline' here mean and why is it a necessary qualifier instead of simply saying assessment should include "investigations to exclude other diagnoses"? We recommend you remove the word "baseline" in this sentence. Many attendees to our community calls discussing the draft Guideline raised concern that doctors (including GPs) did not have the knowledge or experience to fully investigate symptoms.	Thank you for your comment. Baseline has been removed. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry

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				This is confirmed on page 72 line 2 of this Guideline where it states "many healthcare professionals lack the confidence and knowledge to recognise, diagnose and manage it". Evidence Review C p43 line 31 reinforces this, stating that "Patients often felt they needed to take a proactive role in their care by doing their own research to persuade health-professionals to meet their needs, by asking for diagnostic tests, seeking treatment elsewhere, turning to private or alternative health services, and in some cases withdrawing from services and managing symptoms themselves." This comes back to why it is so important specialist services have appropriate medical expertise as part of the staff team, especially when it comes to confirming diagnosis.	out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations
ME Action UK	Guideline	008	011	We are happy with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	008	016	Some attendees to our community calls told us this would be more accurate if it stated: symptoms are new or had a specific onset" instead of "and". They reported that particularly in children and young people, a specific onset could be hard to define, with slow deterioration over time. They told us that requiring symptoms to be new *and* have a specific onset meant they wouldn't receive the support they needed. A simple change from "and" to "or" here would help these people.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong.
ME Action UK	Guideline	008	017	Symptoms: Debilitating fatigability is not defined in this box, whereas the other symptoms have a greater explanation. As the committee has agreed "there is a marked difference between 'normal tiredness' and the profound fatigue caused by ME/CFS and that the term fatigue does not reflect the actual symptoms that people with ME/CFS experience." (Evidence Review D, page 50, line 29)	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change fatigability. This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not

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				We urge the committee to define fatigability in this box. Doing so only in the section on "Terms used in this guideline" is likely to lead to a common understanding of the term fatigue being used, without reference to the specific features that the committee has outlined.	significantly relieved by rest.'. The committee hope this has added some clarity for readers. In addition the definition in the terms used in the guidelines has been edited to provide further clarity.
ME Action UK	Guideline	008	017	Symptoms: During our community call that discussed this draft Guideline, there were more people who agreed than disagreed that the term post-exertional symptom exacerbation was better than post-exertional malaise, however this was not unanimous. Overall, we agree with the committee's assessment that the word malaise underplays the severity and impact of this symptom in people with ME. Our colleagues in the US expressed concern that adding a new term would create yet another long acronym: PEM/PESE. They noted that they are getting traction with US institutions using the terminology PEM at the moment, and felt a change may lead to greater confusion. We published a poll on our social media platforms to assess what term people preferred. Of 406 respondents, 49% supported the term PEM, 43% supported PESE and 8% supported other terms.	Thank you for your comment. Terms used in the guideline After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
ME Action UK	Guideline	008	017	During our community calls, some attendees also said that, in their experience, PESE/PEM was not always delayed, and preferred the wording "can be delayed in onset by hours or days" to "is delayed…". We agree that this symptom is disproportionate to the activity, and has a prolonged recovery time, and support the inclusion of these sentences in the definition.	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.

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ME Action UK	Guideline	008	017	We agree with the inclusion of unrefreshing sleep.	Thank you for your comment.
ME Action UK	Guideline	008	017	There has been debate about the inclusion of cognitive difficulties as a necessary symptom for diagnosis. Some people have told us they did not experience cognitive difficulties at the beginning of their illness, although generally these became more pronounced with time. We published a poll on social media asking about cognitive difficulties in people with ME. Of 500 respondents, 96% had cognitive difficulties at the onset of their illness, 6% did not, and 2% did not have ME. Albeit a minority, 6% is still significant. Overall, we strongly agree with narrower criteria than the 2007 NICE Guideline being utilised. However, we ask the committee to consider how they will mitigate against an initial presentation of ME without cognitive difficulties delaying diagnosis, advice and support. One option raised was the possibility of an atypical ME diagnosis, as is proposed in the International Consensus Criteria. We support the inclusion of a description of cognitive difficulties here, and agree with the specific presentations of cognitive difficulty the committee has laid out here.	Thank you for your comment. The committee are pleased to see that their experience concurs with that of your respondents and maintain that cognitive difficulties are a key symptom in suspecting ME/CFS and are commonly reported in people with ME/CFS. They note that cognitive difficulties (such as brain fog) are described in most of the criteria (7 of the 9) criteria) reviewed in Evidence review D in contrast with orthostatic intolerance (4 of the 9 criteria) supporting further their experience and expertise and this has been added to their discussion in the report. The committee note that while clinicians are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement the guidance does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
ME Action UK	Guideline	009	003	We are unsure if the term 'exclusive' is accurate here, as it implies that the symptoms in Box 1 are all exclusive to ME. This may be true in combination, but individually they are not. Could the committee remove the part in between commas, so that the sentence just reads "Be aware that the following symptoms may also be associated with ME/CFS:"	Thank you for your comment. It is important to note that these symptoms while common to ME/CFS may well be as a result of another condition and should not be automatically attributed to someone's ME/CFS. To address your point at the top of box 1,' All these symptoms should be present' has been added.
ME Action UK	Guideline	009	003	This list is a helpful addition to the symptoms laid out in Box 1, and we strongly support its inclusion in the Guideline. We are surprised to see no mention of gastrointestinal symptoms (nausea, incontinence, constipation and bloating) on this list	Thank you for your comment. Based on the evidence reviewed in evidence review D and on their experience the committee agreed to add gastrointestinal symptoms to the list.

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				though. Evidence demonstrates an increased prevalence of gastro-intestinal symptoms in ME,[1] and both the International Consensus Criteria[2] and the Canadian Consensus Criteria[3] note these symptoms. We recommend adding gastrointestinal symptoms (nausea, incontinence, constipation and bloating) to this list. We also see that gastrointestinal symptoms are noted on page 6, line 22 under "Awareness of severe or very severe ME/CFS", but cannot find evidence to suggest these symptoms are only present in severe or very severe ME. 1. Maes, M., Leunis, J. C., Geffard, M., & Berk, M. (2014). Evidence for the existence of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) with and without abdominal discomfort (irritable bowel) syndrome. *Neuroendocrinol. Lett*, *35*, 445-453. 2. Carruthers, B. M., van de Sande, M. I., De Meirleir, K. L., Klimas, N. G., Broderick, G., Mitchell, T., ... & Bateman, L. (2011). Myalgic encephalomyelitis: international consensus criteria. *Journal of internal medicine*, *270*(4), 327-338. Carruthers, B. M., Jain, A. K., De Meirleir, K. L., Peterson, D. L., Klimas, N. G., Lerner, A. M., ... & Sherkey, J. A. (2003). Myalgic encephalomyelitis/chronic fatigue syndrome: clinical working case definition, diagnostic and treatment protocols. *Journal of chronic fatigue syndrome*, *11*(1), 7-115.	
ME Action UK	Guideline	009	017	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	009	021	We agree with this recommendation that testing should continue, however as we have previously mentioned: Some attendees of our community call to discuss the draft Guideline felt it would be helpful to list investigations that should	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. Taking into consideration the stakeholder comments the

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				be done, whilst others felt this might limit what is done just to those investigations listed. It was generally felt that a list of possible differential diagnoses could be helpful, with a proviso that the list is not exhaustive and the healthcare professional should consider what is necessary to rule out based on symptomatology. We also request that this recommendation notes that co-existing conditions may be present.	committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. In addition the committee have added that ME/CFS should be suspected if the, 'symptoms are not explained by another condition.' The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS and includes the examples you have listed.
ME Action UK	Guideline	010	017 - 021	We strongly agree with these bullet points, particularly the mention of rest which we strongly urge the committee to retain. We recommend adding, after line 19, that "the amount of activity they can manage without triggering PESE may be lower than they initially expect" In our experience, people are often surprised by how tiny activities can cause PESE, especially early on in their illness.	Thank you for your comment. This section is about people with suspected ME/CFS and it is important that the advice recommended and terms used are also relevant to people that may have suspected ME/CFS but are in the end diagnosed with another condition. After considering stakeholders comments the committee edited the recommendations to simplify the wording and for this reason your suggestion has not been included. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on pem and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms.

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					*After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
ME Action UK	Guideline	010	002	It would be helpful to define who this specialist is, and whether the suggestion is to seek advice from an ME specialist, or a specialist in the specific sign or symptom that there is uncertainty about. We support the referral of people with ME to other specialties where there is uncertainty in interpreting signs and symptoms. We particularly urge that symptoms should not be assumed to be ME without thorough investigations.	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
ME Action UK	Guideline	010	004	We are pleased to see an additional section on children and young people with suspected ME here.	Thank you for your comment.
ME Action UK	Guideline	010	007	We support the recommendation to refer children and young people to a paediatrician. However again we recommend that you add a list of differential diagnoses with the proviso that the list is not exhaustive.	Thank you for your comment. The discussion section of Evidence review D- Diagnosis includes a list of differential and co-existing conditions that commonly occur in people with ME/CFS.
ME Action UK	Guideline	010	009	We suggest changing this recommendation to "offer to write to the child or young person's place of education or training…" (our addition in bold). This would ensure that the child or young person, along with their parent or carer, maintains a role in leading their care.	Thank you for your comment. After considering the stakeholders comments this has been edited to, 'work with the child or young person's place of education to support flexible adjustments and adaptions' to be more collaborative. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.

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ME Action UK	Guideline	010	011	We support the inclusion of a section on advice for people with suspected ME.	Thank you for your comment.
ME Action UK	Guideline	010	015	We agree that personalised advice on symptom management should be available.	Thank you for your comment.
ME Action UK	Guideline	010	022	During online and community call discussions, some participants raised concerns that this recommendation could be taken in isolation. Therefore, we recommend that you add to the beginning of this line: "After giving advice on symptoms, energy management, rest and diet, explain to people with suspected ME/CFS…"	Thank you for your comment. The recommendation sits in the section on advice for people with ME/CFS and the committee hope that it would be read in this context. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	011	020 - general	Section 1.8 "Access to care" should be moved to before this section (1.5). This would ensure that health professionals assessing people with ME are aware of the recommendations on access to care.	Thank you for your comment. The access to care section of the guideline refers to people with a diagnosis of ME/CFS your suggestion here is before a diagnosis has been made. The committee agreed it was in the correct place in the guideline and did not move the section.
ME Action UK	Guideline	011	001	We strongly agree with the recommendation that people with suspected ME can return for a review if they develop new or worsened symptoms, and to ensure they know who to contact for advice. However this recommendation puts the onus on the person with suspected ME to manage accessing an appointment for diagnosis and referral to specialist care. Considering the long term implications of ME, the physician (most likely GP) should proactively follow up with the person at 3 months. Other guidelines by NICE give clear recommendations of timescales that should be adhered to in the provision of care, and this committee has found that early diagnosis and information	Thank you for your comment. This recommendation has been edited to,' Reassure them that they can return for a review *before that* if they develop new or worsened symptoms, and ensure they know who to contact for advice'. This clarifies that the person is reviewed if they have persistent symptoms after 3 months.

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				can improve outcomes, it is vital the committee makes an explicit recommendation that the healthcare professional arranges a follow-up appointment at 3 months in order to reassess and refer forwards to the specialist team for confirmation of diagnosis if the person continues to experience all of the persistent symptoms in Box 1. Change this to: "Explain to people with suspected ME that their diagnosis can only be confirmed after 3 months of persistent symptoms, and arrange a follow up appointment for that time. Reassure them that they can return for a review before then if they develop new or worsened symptoms, and ensure they know who to contact for advice."	
ME Action UK	Guideline	011	003	There appear to be three levels of diagnosis in this Guideline. Provisional diagnosis for those with suspected ME, diagnosis at 3 months, and then confirmation of diagnosis by a specialist team. The differential diagnosis seems more complex than is reasonable to expect a GP to do and not miss comorbidities or rarer alternatives. Recommendations 1.4.2 and 1.5.1 appear to define a referral pathway, with confirmation of diagnosis by a specialist. However this could be made clearer, and we therefore recommend adding a new step under Assessment and care planning by a specialist ME team (section 1.5) that states "Confirm diagnosis or refer for further investigations." We have made this recommendation as a separate comment on section 1.5 as well. .	Thank you for your comment. After considering the stakeholder comments on the guideline sections on suspecting and diagnosing ME/CFS the committee agreed to make some edits to the recommendations and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added

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					examples of investigations to be done when suspecting ME/CFS. In recommendation 1.4.2 'to confirm their diagnosis has been added. Recommendation 1.5.1 includes confirmation of diagnosis and as part of the assessment a medical assessment is listed. This would include appropriate investigations for comorbidities or differential diagnosis.
ME Action UK	Guideline	011	007	For many long term conditions GPs will often refer, with a suspected diagnosis, to a specialist team, seeking a more detailed assessment, which may include a range of specialist tests, confirmation and a management plan which they will be part of. Evidence Review I p24 line 5 states: "The committee acknowledged that GPs did not have enough time to carry out the assessments needed to confirm a diagnosis of ME/CFS or to develop a management plan in a single standard appointment. The committee recommended that once someone with suspected ME/CFS has had persistent symptoms indicating ME/CFS for 3 months the person should be referred to a specialist team for confirmation of the diagnosis." However this recommendation is unclear, and must be explicit that the diagnosis of ME should be confirmed by a specialist. Change this to: "Refer adults directly to a specialist ME team to confirm the diagnosis of ME and to develop a management plan."	Thank you for your comment. After considering stakeholder's comments the committee have edited this recommendation to clarify that referral to the ME/CFS specialist team is to confirm the diagnosis and to develop a care and support plan.
ME Action UK	Guideline	011	009	We agree that it is important that paediatric specialist team members should be experienced in ME, however to create the change in service provision truly needed this sentence must also specify that paediatric specialist team members have training in accordance with this Guideline.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the

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				Change to: "If ME is diagnosed in a child or young person after assessment by a paediatrician (based on the criteria in recommendation in 1.2.3), refer them directly to a paediatric specialist team with experience in ME and training in accordance with this Guideline to develop a management plan."	recommendations in the training for health and social care professionals section of the guideline.
ME Action UK	Guideline	011	015	The pathway to a confirmed diagnosis is unclear here, with a simple reference to "After confirming diagnosis of ME/CFS". This needs to be a step of its own, that is taken after the holistic assessment, not before the clinician even takes a history. Add a new recommendation after these bullet points: "Confirm diagnosis or refer for further investigations."	Thank you for your comment. The committee agree this is not clear and have revised the recommendation to, 'carry out and record a holistic assessment to confirm a diagnosis and inform the care and support plan.'.
ME Action UK	Guideline	011	017	We are concerned that this recommendation does not specify what "relevant symptoms" are. More guidance needs to be given on this to ensure that the correct questions are asked and relevant history is explored thoroughly in order to identify symptoms.	Thank you for your comment. Relevant symptoms refers to the any symptoms relating to ME/CFS. As with all medical assessments clinical judgement should be used and appropriate to the person having the assessment.
ME Action UK	Guideline	012	013 - 030	We agree with all the bullet points here, We particularly agree with the recommendation that all people with ME should have "details of the health and social care professionals involved in the person's care, and how to contact them." We have only one comment on the sections of the Guideline referred to in the symptom management bullet point - see next point	Thank you for your comment.
ME Action UK	Guideline	012	025 - 026	The current reference to recommendations for symptom management excludes the recommendations on orthostatic intolerance which start at section 1.11.24. The recommendations should be changed to start at 1.11.24. The current reference to recommendations on symptom management includes recommendations on CBT (recommendation 1.11.50). CBT should not be included as it is	Thank you for your comment. The links have been updated.

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				not a way of directly managing symptoms of ME. Recommendations should be changed to end with 1.11.42	
ME Action UK	Guideline	012	004	We are concerned that the language of psychosocial wellbeing could be seen as reductive here, excluding areas such as housing and benefits, and for this reason believe "overall wellbeing" would be a more appropriate term. We agree with the language of "impact of symptoms on…", and are pleased to see the committee considering it in this way. Reword to "the impact of symptoms on their overall well-being."	Thank you for your comment. After considering the range of stakeholder comments, this bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing'.
ME Action UK	Guideline	012	010	We support the recommendation to develop a personalised management plan based on the holistic assessment of the person's needs	Thank you for your comment.
ME Action UK	Guideline	013	001	We strongly agree with the recommendation that the specialist team should recognise the person with ME is in charge of the aims of their management plan.	Thank you for your comment.
ME Action UK	Guideline	013	009	The recommendation states that copies of the management plan should be given to the person: we suggest that there should be additional text here saying the copy of the management plan should be provided in paper and online to the person with ME. This would ensure it is accessible.	Thank you for your comment. The committee recommend that information should be provided in a variety of formats in the first recommendation in the information and support section.
ME Action UK	Guideline	013	012	We are concerned that the recommendation of home visits for the holistic assessment is only for those with severe or very severe ME. This service should be available for those with moderate ME who may be unable to visit the specialist team in person. We cannot see any evidence in Evidence Review A or Evidence Review G that supports the recommendation only to offer home visits for assessments to severe/very severe.	*Thank you for your comment.* *Home visits* The committee agreed that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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ME Action UK	Guideline	013	012	This recommendation should specify who within the specialist team should carry out home visits in order to ensure that it is a member of the team with relevant skills and experience.	Thank you for your comment. *Training* The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. In Evidence review I- multidisciplinary care the variation in the delivery of ME/CFS specialist services is discussed by the committee. The committee agreed that the decision about who would carry out home visits is a local service decision.
ME Action UK	Guideline	013	013	The box below this line appears to reference the wrong evidence review	Thank you for your comment. This has been amended.
ME Action UK	Guideline	013	016	We are concerned that this section on Information and Support does not address the issue that non-English speaking people face in obtaining a diagnosis and accessing care - see (Evidence Review C p72 line 1-10). Although there is reference to the relevant NICE Guideline in this section, we suggest that this important point should be highlighted in the Guideline with the addition of a sentence such as that used in the relevant Guideline: "Difficulties with reading, understanding or speaking English are addressed so that the patient is able to participate as fully as possible in consultations and care."[1] Patient experience in adult NHS services: improving the experience of care for people using adult NHS services | Guidance | NICE	Thank you for your comment. As you note this recommendation includes the link to the NICE guidelines on patient experience in adult services and this has further detailed information on communication. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable.

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ME Action UK	Guideline	014	005 - 007	It is good to see alternative formats suggested for providing information to children and young people, but not all are suitable for those with severe ME who may have noise and light sensitivities.	Thank you for this comment and information.
ME Action UK	Guideline	014	023 - 024	Wording on recovery should be amended to make it clear that even those who recover or have a long period of remission from ME have to live their lives with caution so they do not have a relapse. The wording should also say 'most' will need to adapt (rather than 'many').	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
ME Action UK	Guideline	014	026 - 027	We agree with the wording that ME can have a major impact on the people's lives, however to then state that "they may need to adjust how they live" underplays the significant debilitation even people with mild ME suffer. We request the committee changes this to: "can have a major impact on people's lives, including their daily activities, family and social life, and work or education, and usually requires significant adjustments in how they live"	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
ME Action UK	Guideline	014	002	We are concerned that this recommendation does not consider the needs of children or young people with severe or very severe ME. The word 'symptoms' should be added after 'any disabilities' to make sure that the needs of those with severe ME are considered. Edit the second sentence to: "Use interactive formats tailored to their individual needs, such as:"	Thank you for your comment. Symptoms has been added. The committee considered the recommendations sets out the individual needs to be considered, 'take into account their age and level of understanding, symptoms and any disabilities or communication needs'.
ME Action UK	Guideline	014	004	The evidence does not support the recommendation of group discussions for children as a format for providing information to them as the evidence cited is based on studies of adults. See Evidence review A p25 line 14-15 for evidence on positive benefit	Thank you for your comment. The committee disagree the evidence does show that children and young people like to meet in groups, where appropriate and this reflected their experience.

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				of group sessions for adults. There is evidence (Evidence Review A p32 line 49) that young people find it beneficial to meet and talk to "others with CFS" , but this does not support the recommendation of group discussions as a format to provide information to children and young people.	
ME Action UK	Guideline	014	016	We support the recommendation to explain that ME is a 'fluctuating medical condition' and are pleased to see this explained here. We would like to see this emphasised in subsequent sections, particularly the section on Access to care page 17 line 20.	Thank you for your comment. The importance of ME/CFS being a fluctuating condition is also highlighted in the recommendations in the principles of care and energy management sections and in the rationale for the access to care recommendations. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As noted fluctuations is reinforced throughout the guideline and for this reason your suggestion has not been added to the recommendations here.
ME Action UK	Guideline	014	029	It is apparent that the common theme running through all of these triggers is overexertion of some description. It would be helpful to explicitly include overexertion here as a trigger. While it is helpful to include childbirth as an example of a stressful event (as mentioned in the Equality Impact Assessment) it would be good to include other common triggers too. e.g. "Examples include traffic accidents, major operations involving general anaesthesia and childbirth"	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples were considered potentially misleading information and not always a trigger and as you have commented there are other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
ME Action UK	Guideline	015	006	We fully support referring people to support groups and suggest that these bullet points are expanded to address the issues faced by black and minority ethnic groups. Evidence Review C p17 and p22 identifies the specific issues faced by the BME community. We suggest adding a bullet point to this list saying "community outreach groups which work with services to help and support	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence

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				black and minority ethnic groups to access healthcare, community and other resources".	was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group, and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
ME Action UK	Guideline	015	008	Information on financial support is vital for people with a chronic illness and we are pleased to see it included here, but it is very rare that medical or social care staff can keep up with the ever changing landscape of benefits. It is therefore important to also signpost to organisations that can provide tailored advice, such a Citizens Advice Bureau. We suggest adding "and signpost or refer them to other organisations that provide advice and support on these areas, such as Citizens Advice Bureau".	Thank you for your comment. The committee agree that signposting to benefits is important but agreed not to add examples of organisations, as with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.
ME Action UK	Guideline	015	009	The rationale for this section refers to the importance to patients of having information for people with ME to share with 'employers' (Guideline p54 line 23), but no mention of this information is made in section 1.6 Information and Support p13. Recommendation 1.6.7 says: "Give families and carers of people with ME/CFS information about the condition and ways they can help the person." Please add a further recommendation saying: "Give people with ME/CFS information suitable for sharing with	Thank you for your comment. As you note section 1.9 has further information on supporting people with ME/CFS in work, education and training and sharing information with employers. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later and for this reason your suggestion has not been added to the recommendation.

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				employers (see recommendations section 1.9 on supporting people with ME/CFS in work, education and training)"	
ME Action UK	Guideline	015	011	We strongly agree that social care should be discussed with the person with ME, and that a referral to social services should be offered.	Thank you for your comment.
ME Action UK	Guideline	015	023	We agree with these recommendations on supporting families and carers of people with ME.	Thank you for your comment.
ME Action UK	Guideline	016	005	Although we recognise the good intentions behind including a safeguarding section to guard against past abuses by health and social work professionals who do not have expertise with ME, this section could be misused as the safeguarding approach taken for ME patients has been in the past. Univadis, a publication and resource for health professionals, has produced an <u>ME/CFS clinical guidance summary</u> based upon this draft guideline.[1] As one of 6 key bullet points on the management of ME/CFS they state "Conduct safeguarding assessment." There is no qualifier that this should only be done when required. It is stated as part of the management approach for all people with ME. This may be a misinterpretation of the Guideline, however it demonstrates how easily this section can be misused. The issue of children's families being threatened by social services with the accusation of Fabricated or Induced Illness(FII)/Munchausen by proxy must be addressed but this section is unclear in its intent. An explicit acknowledgement of the historical misuse of safeguarding must be added towards the end of the section on "Principles of care for people with ME/CFS" with a statement that an ME diagnosis is NOT grounds for a safeguarding assessment, sectioning or child protection order. In Evidence Review B p57 line 24 "The committee agreed it was important that recommendations address some of the common	Thank you for your comment. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. To clarify this point. As you note the importance of this section is discussed at length in the committee discussion in Evidence review B. When considering the stakeholder comments and the structure of the guideline the committee agreed that the safeguarding section was already appropriately placed.

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				misconceptions that may have led to child protection concerns, and to provide guidance on this topic." In the feedback we have received, parents of children with ME are very concerned that instead of addressing common misconceptions, by inserting a section on safeguarding, the committee are inadvertently implying that abuse of children with ME is common, contrary to any evidence to suggest this. We have heard too often that the NICE Child Maltreatment Guideline[2] has been misused against children and young people with ME and their families. For a poorly understood disease such as ME section 1.1 on Physical Symptoms has been used to launch safeguarding investigations at a disproportionate rate, leading to accusations of Fabricated and Induced Illness against families of children and young people with ME.[3] FII is a rare form of child abuse,[4] with any connection between this rare occurrence and ME entirely unfounded in evidence. We very strongly urge the committee to clearly state that this issue lies with misuse of safeguarding procedures, not with abuse of children with ME by parents. Considering the above, we ask the committee to take action to mitigate against seriously damaging unintended consequences of this section. While there have been varying views expressed in discussing this section of the Guideline, with some pleased to see the inclusion of certain recommendations, we have ultimately concluded, in consultation with experts in this area, that a standalone section on safeguarding in a medical Guideline is not the way to address this.	

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				We therefore recommend moving recommendations within this section, many of which are important and highly welcomed, into the section on principles of care. 1. O'Shea, D. New NICE guidance on chronic fatigue syndrome: the key points. (2020) *Univadis* https://www.univadis.co.uk/viewarticle/new-nice-guidance-on-chronic-fatigue-syndrome-the-key-points-732697 2. Child maltreatment: when to suspect maltreatment in under 18s (2017) *NICE* https://www.nice.org.uk/guidance/cg89 3. Colby, J. False Allegations of Child Abusein Cases of Childhood MyalgicEncephalomyelitis (ME) (2014) *Argument and Critique* https://www.tymestrust.org/pdfs/falseallegations.pdf Fabricated or Induced Illness (2019) NHS https://www.nhs.uk/conditions/fabricated-or-induced-illness/	
ME Action UK	Guideline	016	006	Neither the MS or Childhood Asthma Guideline or the majority of Guidelines on individual biomedical illnesses have a safeguarding section. It is counterproductive to have one here as this section of the draft Guideline is already being interpreted as an alert that ME indicates safeguarding concerns. See Univadis clinical guidance summary where they recommend, on the basis of this draft Guideline, conducting a safeguarding assessment for all people with ME. By stating that "safeguarding assessments… should be carried out…" this committee appears to be recommending a terrifying and dangerous protocol. If retained this recommendation should state: *"If a* safeguarding assessment *is required* in people with confirmed or suspected ME/CFS it should be carried out or overseen by health and social care professionals who have	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.

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				training and experience in ME/CFS *in accordance with this Guideline*." The misuse of safeguarding procedures has caused distress to families and children and exacerbation of symptoms for people with ME, and we understand this is what the committee is attempting to ward against. However, this section has already done the opposite. Considering that, and in discussion with other experts in this field, we do not think a separate section on safeguarding should be included, and urge the recommendations on safeguarding to be moved into the section on principles of care, with appropriate wording to clarify that the committee's concern is about misuse of safeguarding procedure by professionals. Evidence Review A p44 line 3 - 'The committee considered that some people may be reluctant to or have reservations about engaging with social care support services due to previous disbelief about the severity of the illness and the level of impact on day-to-day functioning. They noted there are sensitivities in this area, particularly with children and young people and their families.'	
ME Action UK	Guideline	016	008	We would welcome staff who have received training based on the new guidance, however this must be made clear to ensure the change in paradigm that this draft Guideline lays out. Any change in approach to managing ME, hinges on both the content of new training and the ability of those undertaking it to accept and alter their views accordingly. They need to recognise and agree that "ME/CFS is a serious, chronic, complex systemic disease that often can profoundly affect the lives of patients and ... is not, as many clinicians believe, a psychological problem."[1]	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.

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				In a quote from Supporting Documentation Appendix 1, a young research participant says "The specialist person didn't listen to me, she even wrote things that weren't right, she was always trying to make things sound better than they were. She made me feel bad, I hated going." This type of experience must never happen again. Add the section in bold: "who have training in accordance with this Guideline and experience in ME." Komaroff, A. L. (2015). Myalgic encephalomyelitis/chronic fatigue syndrome: A real illness. Annals of internal medicine, 162(12), 871-872. https://www.acpjournals.org/doi/10.7326/m15-0647	
ME Action UK	Guideline	016	009	We strongly agree with the inclusion of this sentence in the Guideline, and the implied recognition of wrongful allegations or abuse or neglect. However this recommendation as it stands will not stop people with severe or very severe ME from being wrongly sectioned, as has happened to some in our community. Sectioning in the UK is based upon the person having a "mental disorder" (Mental Health Act 1983). Based on our experience in this community, people with severe or very severe ME are in danger of having their physical symptoms misinterpreted as psychological problems e.g. an inability to swallow or digest food being wrongly attributed to an eating disorder. Any professional involved with these patients should have extensive training on the problems that people with severe and very severe ME can suffer and on the new Guideline. To ensure people with ME are not wrongly sectioned, there must be an additional statement here that simply says "ME is not a mental disorder."	Thank you for your comment. The first recommendation in the guideline raises awareness that ME/CFS is a complex, chronic medical condition affecting multiple body systems and its pathophysiology is unclear and covers your suggestion. . The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. When considering the stakeholder comments and the structure of the guideline the committee agreed that the safeguarding section was already appropriately placed.

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				This will ensure that those who do have a severe coexisting mental disorder can receive the treatment they require, while those without a coexisting mental disorder will not be wrongly sectioned. This recommendation would therefore become: "Recognise that people with ME/CFS, particularly those with severe or very severe ME, are at risk of their symptoms being confused with signs of abuse or neglect. ME/CFS is not a mental disorder." As the recommendations on safeguarding laid out in the draft Guideline have already been misused we recommend that this should instead come under "principles of care" section to avoid further suffering being inflicted on people with ME and the Safeguarding section removed.	
ME Action UK	Guideline	016	012	We strongly agree with this recommendation in principle. However in practice many healthcare professionals retain incorrect assumptions about ME based upon stigma and bad science. Professionals involved in the care of people with ME should receive training that is in accordance with this Guideline before they can continue or start working with people with ME, especially in an area where the patient's wishes may be overridden. We urge the committee to add the bolded wording: "If an assessment under the Mental Health Act 1983 or the Mental Capacity Act 2005 is needed, involve health and social care professionals who have training and experience in ME/CFS in accordance with this Guideline.."	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	016	017	This section on Children and Young People under Safeguarding was undoubtedly put here to protect children, young people and their families from unjustified safeguarding procedures. Unfortunately, it gives the impression that safeguarding concerns	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and

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				are indicated in people with ME. This is already being briefed to doctors; e.g univadis.co.uk. We can find no other Guideline for a biomedical illness that includes a safeguarding section and having it here gives the impression that safeguarding procedures are justified and should be commonplace in ME care, even with the caveats. We strongly urge the committee to remove the Safeguarding section. If it is not removed we recommend that a statement is added saying "Be aware that a diagnosis of ME/CFS in a child or young person is not grounds for suspecting abuse or neglect." Due to the misuse of this section, we also urge the committee to move the recommendations in 1.7.6 to the section on principles of care.	understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. When considering the stakeholder comments and the structure of the guideline the committee agreed that the safeguarding section was already appropriately placed.
ME Action UK	Guideline	017	008	Saying "not necessarily a sign of abuse" leaves a broad range of doubt to the interpretation from "unlikely to be" to "may be but are not definitely". We suggest rewording to: "Recognise that the following are established features of ME and the following should not be taken as a sign of abuse or neglect in children and young people with confirmed or suspected ME:" Having this section under Safeguarding implies that abuse and neglect is a problem to be addressed for children and young people with ME and will be used to continue making unfounded allegations about this vulnerable group. It would be less damaging to children, young people and their families who have suffered stigma and prejudice if this section was moved to "Additional principles of care for children and young people with ME/CFS" and we recommend that this is done.	Thank you for your comment. It is important that children and young people at risk of abuse and neglect have the support they need, stating that these are not or never signs of abuse or neglect could endanger some children and young people. When considering the stakeholder comments and the structure of the guideline the committee agreed that the safeguarding section was already appropriately placed.

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ME Action UK	Guideline	017	020	Section 1.8 Access to Care should be moved to before Section 1.5 Assessment and Care Planning. This would ensure that the specialist teams treating ME patients are aware of how to ensure that people with ME can access their services. .	Thank you for your comment. This section is about access to care for people with ME/CFS and as such fits after the assessment and care and support planning section where diagnosis is confirmed.
ME Action UK	Guideline	018	001	The recommendation on adapting appointments is very useful. GPs and patients find the constraints of 10 minute appointments do not work when dealing with a complex illness such as ME so should be guided to offer longer appointments to this group of patients. Evidence Review C line 32 - 'Patients highlighted the limited time for consultation as a barrier to appropriate care provision and another reason for seeking support outside the NHS. Health professionals recognised that a 10-minute consultation can be challenging due to the variety and complexity of ME symptoms.	Thank you for your comment and information.
ME Action UK	Guideline	018	008	We request that email is added to the list of providing care flexibly as some people can't speak but can write emails in a paced manner to communicate with HCPs.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Action UK	Guideline	018	010	The 'do not discharge' recommendation is warmly welcomed. We would add that HCPs should explore other ways that people with ME can access healthcare; e.g. video or phone.	Thank you for your comment. The previous recommendation includes how care can be provided flexibly and includes online or phone consultations. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	018	013	Thank you for including this important point. People with ME are rarely seen at their worst and often ration energy to attend	Thank you for your comment. This recommendation raises awareness about the reasons people may miss an appointment not about follow up after an

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				appointments. We suggest following up several days after any appointment to check if it has triggered PESE.	appointment and for that reason your suggestion has not been added.
ME Action UK	Guideline	018	15	The word 'fear' is unhelpful and inaccurate. We request that it is replaced by 'possibility of' or 'concern regarding'' or "risk"	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
ME Action UK	Guideline	018	017	This is a very welcome addition to the Guideline as patients are likely to have prepared for the appointment with preemptive resting and will do less in the days afterwards to minimise PEM/PESE.	Thank you for your comment.
ME Action UK	Guideline	018	020	The proactive and flexible recommendations for people with severe and very severe ME are welcome. We ask you to add that the time of day that appointments are offered should also accommodate the needs of this group. We would like to stress the importance of home visits for these patients who may be not able to access telephone or video appointments. As one mother of a severely ill young woman said, 'in seven years of severe illness, my daughter has had no home consultations or visits from NHS specialist ME staff. However, we strongly urge that this flexibility is offered to people with moderate ME as well who are defined in the Guideline as having 'reduced mobility and are restricted in all activities of daily living' and often have great difficulty accessing care. In any other illness this level of disability would be regarded as severely affecting their lives and we feel that 'moderate' underplays the level of disability that this group experiences. In the supporting documentation Appendix 1 Children and Young People (p18 line 27) ME11 stated: "I think doctors should do home visits if the patient isn't well enough to go. Because a lot of the times like the doctors ... like we've had to travel to my consultant before because they've moved him, and at times it's been tough getting to him cos of I've just been unwell."	Thank you for your comment. The access to care recommendations do include that service providers should ensure people with ME/CFS can access health and social care services by adapting the timing, length and frequency of all appointments to the person's needs. To note, after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. The access to care section of the guideline with information on flexible appointments is directly linked to. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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ME Action UK	Guideline	019	001	We welcome this suggestion and would add that flexibility around timing of routine tests should be offered.	Thank you for your comment. This recommendation is about where care will be provided and aiming for a low stimulus environment and not about how care is provided for this reason your suggestion has not been added.
ME Action UK	Guideline	019	004	We also urge that people with ME who are ill enough to need hospital care need a single room regardless of their illness level as the extra exertion, noise, light and medical examinations on top of any comorbid illness can cause a relapse and severe PESE.	Thank you for your comment.
ME Action UK	Guideline	019	008	We welcome these recommendations on hospital care for people with severe or very severe ME but urge that they are also offered to people with mild or moderate ME. The evidence from review A quoted below applies to all patients with ME. Evidence Review A p26 line 30 - "Patients who had hospital care also described their need for designated wards for ME, with environments adapted to their needs, as in keeping light and noise levels low. Some highlighted the limited time for consultation as a barrier to appropriate care provision and another reason for seeking support outside the NHS."	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or hospital can be difficult. This section does make a recommendation for all people with ME/CFS and includes that any difficulties in accessing hospital care should be discussed and gives some examples of what should be considered. These are expanded on for people with severe or very severe ME/CFS taking into account there are further challenges to consider.
ME Action UK	Guideline	019	020	The Guideline says to 'aim to provide a single room if possible' for people with severe or very severe ME. However, a single room is essential for a person with severe or very severe ME, as it is impossible to keep light, sound, and movement to a low level in a ward setting. We would urge that these patients are a priority for a single room and reword the recommendation to 'provide a single room as a priority'.	Thank you for your comment. The committee recognise the importance of people with severe or very severe ME/CFS having a low stimulus environment in hospital and this includes a single room but they also recognised there may be occasions where this is not possible.
ME Action UK	Guideline	019	021	The advice on keeping stimuli to a minimum is welcome and we thank the committee for including this. We suggest one addition, there should be reference to the fact that dimming lights may not be enough and windows will need to have blinds drawn and also may need additional measures such curtains to block out sufficient light as blinds on their own may not be adequate.	Thank you for your comment. These are examples of what to consider in facilitating a low stimulus environment in a hospital, it is not meant to be exhaustive and for this reason your suggestions have not been added.

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				Hospitals may need to work with families and carers to determine the level of light that the person with ME can withstand.	
ME Action UK	Guideline	020	020	We welcome the recommendation for provision of aids and adaptations without delay. This will help people avoid PEM/PESE and relapses.	Thank you for your comment.
ME Action UK	Guideline	020	023	We warmly welcome this recommendation.	Thank you for your comment.
ME Action UK	Guideline	020	026	We welcome this recommendation on providing aids and adaptations for people with moderate, severe or very severe ME. Electric wheelchairs should be specified as the exertion involved in propelling a manual wheelchair can make their use impossible for people with ME. We also recommend that this provision is extended to include people with mild ME if needed. Levels of ability can fluctuate daily and aids and adaptations for people with mild ME/CFs can prevent PESE, relapses and degradation of function.	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.
ME Action UK	Guideline	021	020 - 022	A balance of activities is important for children and young people. We would like to see these listed so there is clarity around the subject and for this to include education and training, home and family, hobbies and social activities.	Thank you for your comment. The committee agree and further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion.
ME Action UK	Guideline	021	004	We welcome the advice to people with ME that there may be times when they are unable to continue with work or education, some people find that going back to work, school or college worsens their symptoms and they may be able to access reasonable adjustments or adaptations. We would strengthen this wording as in the 'Living with the impact of ME' survey undertaken by Action for ME in 2019, 83% of people had to stop or reduce work and 77% had to stop work entirely. We suggest rewording from “there may be times when they are unable to continue with work or education” to 'there will often be times when they are unable to continue with work or education.'	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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ME Action UK	Guideline	021	011	We welcome this suggestion. Liaising with employers etc is a valuable and welcomed service. We request that insurers be added to this list for people unable to return to work. The Department of Work and Pensions should be included in this list as they are a gatekeeper for benefits and disbelief in ME as a serious disease means that people are often denied benefits. Due to the fluctuating nature of ME people often struggle to gain accommodations from employers or benefits from the DWP as illustrated in Evidence Review C p72 line 27: "The committee discussed that the unpredictability of the severity of people's symptoms can sometimes prevent reliable planning ahead meaning that scheduled appointments (or work) may be missed or cancelled with little notice."	Thank you for your comment. The remit of NICE does not extend to providing guidance for the Department for Work and Pensions (DWP) and insurance companies but the committee would hope that any organisations who engage with people with ME/CFS would use this guideline as an example of best practice.
ME Action UK	Guideline	021	015	This is an important provision. However an additional recommendation is required here. Children and young people with ME are often pressured to increase school attendance as shown in the following evidence: Supporting Documentation Appendix 1 p13 line 3 "Often the school concerned would initially require the participant to attend lessons or restrict the ability to rest." Evidence Review A p33 line 13 - "Young people felt that better support from education systems could have helped. They described schools and colleges as inflexible, unhelpful, un-empathetic and invalidating." Evidence Review A p33 line 21-23 - "letter provided by the 'CFS/ME' service confirming a diagnosis enabled mothers to	Thank you for your comment. The remit of NICE does not extend to providing guidance for the training and education services but the committee hope that schools would work with healthcare professionals about adjustments for children and young people with ME/CFS.

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				legitimately take their child out of school, request funding for home schooling and more generally inform and gain support from teachers when managing reduced attendance." Evidence Review C p55 line 39 - "Both teachers and families identified the diagnosis as a catalyst to the school taking the health concerns seriously and implementing the necessary support. Teachers emphasised that at an organisation/policy level, teachers needed this formal diagnosis to implement treatment recommendations, such as reduced timetables." Further to this, specialist services are often seen as unhelpful or as doing harm to children and young people with ME, as Evidence Review A p30 line 45 states: "Young people appeared to experience difficulty with a lack of understanding and awareness around the condition from medical professionals involved." In the patient survey "Your Experience of ME Services" by #MEAction UK, the overwhelming experience of respondents of all ages attending specialist clinics was negative, a trend that is especially pronounced in the experience of children and young people. There are over 140 negative comments from young people or their carers recounting their treatment by the specialist clinics and fewer than 10 positive or neutral ones. Children, young people and their families report to us that they need to attend services to obtain letters giving them access to home/online tuition or to reduce attendance, as local authorities will commonly refuse to accept letters that are from their GP. This is problematic as access to consultants can be limited or take a long time, delaying access to the support children and young people require. Guidance should be provided to education authorities and local authorities that a letter from a GP is sufficient evidence that a child is either 'unfit for school' or needs accommodations.	

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				We therefore urge the committee to add an additional recommendation stating that: "Training and education services should accept letters from either GPs or consultants that the child or young person is "unfit for school" or requires accommodations."	
ME Action UK	Guideline	022	003	A flexible approach to training and education is an excellent provision. Acknowledging the value of home or online education as a means of ensuring that children and young people can access education is very welcome as this has been a major barrier for children and young people with ME. We are pleased to see this included considered the important evidence identified, such as: Supporting Documentation Appendix 1 p13 line 3 - "Often the school concerned would initially require the participant to attend lessons or restrict the ability to rest." Evidence Review A p46 line 3 - "It was highlighted by the committee that there is a legal responsibility to ensure children receive an education, but this does not mean that they must attend a school." Evidence Review C p53 "There is often a lack of sufficient or direct communication between schools, families and health-care professionals, implicating the care of children with ME/CFS and the importance of such an ongoing communication across settings is acknowledged by all parties."	Thank you for your comment.
ME Action UK	Guideline	022	006	Advice on applying for education, health and care plans will be welcomed by parents and carers. The inclusion of a note on confirming the eligibility of children with ME/CFS for EHCPs is needed here along with notification of the same to local authorities.	Thank you for your comment. The previous recommendation in the section covers the provision of information.

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ME Action UK	Guideline	022	014	We acknowledge the lack of evidence identified to inform recommendations on multidisciplinary care, and that therefore the committee has made these recommendations based upon their own experience and consensus views. However these recommendations on multidisciplinary care do not provide the clarity required for commissioning of services, and do not align with the recommendation that the specialist team should confirm diagnosis of ME. There is no explicit mention in this section that a physician should be included in the team, although this will be necessary to confirm diagnosis. Where evidence cannot be found for a specific disease it is appropriate to explore more broadly. A report by the Academy of Medical Royal Colleges found that "the consistency of the association between consultant involvement and improved outcomes across many studies in many specialties is compelling." On the basis of further systematic review they conclude "there is considerable internationally shared professional knowledge, expert opinion and considerable secondary evidence to support decision-making with regard to future policy making on consultant-delivered care. This body of knowledge and expertise recognises the complications that arise from a lack of consultant presence, failure to care by non-consultant staff and it supports the concept of consultant-delivered care." Evidence from surveys of people with ME supports the appointment of physicians to any multidisciplinary specialist team.	Thank you for your comment. As you comment the committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but the committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. In addition the committee have After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the design and delivery of services, which can be determined locally.

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				An ME Association survey found that when asked, "Which health professionals and organisations do you want to be involved?", the GP was most favoured, then a consultant physician. #MEAction UK's survey report "Your Experience of ME Services", undertaken in response to this committee's call for evidence, found that when respondents were asked who they would most want on a multidisciplinary team "consultant was the most common choice, with 76% choosing this as one of their top 3 [professions]." In both surveys, psychologists were amongst the least preferred profession to support management of this illness. Similar sentiment was also expressed by participants of the community calls #MEAction UK held to discuss this draft Guideline, who felt that specialist teams should not be led by psychiatrists or psychologists. Evidence Review I p24 line 5 states: "The committee acknowledged that GPs did not have enough time to carry out the assessments needed to confirm a diagnosis of ME/CFS or to develop a management plan in a single standard appointment. The committee recommended that once someone with suspected ME/CFS has had persistent symptoms indicating ME/CFS for 3 months the person should be referred to a specialist team for confirmation of the diagnosis." This acknowledgment is very important to the make-up of a multidisciplinary team, as it requires there is a physician with expertise in ME in order to confirm diagnosis.	

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				This committee must therefore add an explicit recommendation for the presence of at least one physician, preferably a consultant, within every multidisciplinary team. We also note that the committee could find no evidence as to which specialty ME should be managed under, and the input we've received from community members on this varies widely. We therefore ask the committee to consider a research recommendation on which specialty should take managing people with ME.	
ME Action UK	Guideline	023	007	We strongly agree with the inclusion of a named contact to help people with ME access support. This is particularly important during a relapse and should go some way to stop people with ME being forgotten by the medical establishment, particularly those with severe ME.	Thank you for your comment.
ME Action UK	Guideline	023	012	We strongly agree with the inclusion of a named contact to help children and young people with ME access support. This is particularly important during a relapse and should go some way to stop children and young people with ME being forgotten by the medical establishment, particularly those with severe ME. It should also be used to ensure that children are not refused education due to not being able to attend school.	Thank you for your comment.
ME Action UK	Guideline	023	012	Evidence Review I page 25 line 10 says: "The committee noted this was particularly important for children and young people and they should be involved in the decision making about their key worker." (our emphasis) We recommend adding the part in bold to this recommendation: "Provide parents and carers of children and young people with ME/CFS with details of a named professional in the specialist team who they can contact with any concerns about their child's health, education or social life. Involve children and young people with ME/CFS in choosing this named professional."	Thank you for your comment. As you comment the committee noted the importance of involving children and young people in their decision making about their named contact in the discussion section however the committee recognised that this may not always be possible or practical and did not put this into the recommendation.

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ME Action UK	Guideline	023	017	Transition to adult services for young people with ME is often very slow or non-existent and the care provided is unsuitable to their needs. In a recent community call one parent who has struggled to get any care for their adult child remarked, "Transitions from paediatric care to adult care is a huge issue. A good paediatrician can coordinate care, but this disappears in adults ….. and GPs don't have the same authority and links that consultants have." This means that there is no joined up approach to care, which has a particularly negative impact on managing comorbid conditions. We urge that young people can opt to remain under the care of their existing team until a suitable care pathway is found for them.	Thank you for your comment.
ME Action UK	Guideline	024	004	We strongly agree with including this statement but are very surprised it doesn't come with a related research recommendation. We hope you will rectify this major omission.	Thank you for your comment. Medicines The committee recognised the lack of research in medicines but did not identify any one medicine to prioritise for research and as such did not make any research recommendations on this topic. Non -pharmacological research Based on the evidence the committee recognised that people with ME/CFS often want information and support on how to manage their ME/CFS symptoms and decided to make research recommendations in the areas where there was an absence of evidence (sleep and dietary strategies, and self-monitoring techniques).
ME Action UK	Guideline	024	006	We are pleased to see energy management forming the basis for other recommendations.	Thank you for your comment.

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ME Action UK	Guideline	024	011	The statement "with" support from a healthcare professional is inaccurate. For many, strategies around energy management are learned and undertaken alone. We cannot find evidence that support from a healthcare professional is a necessary part of energy management. We strongly agree that people should have support from appropriately trained healthcare professionals where they want it, but think this language should be changed from "with" to "can include".	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
ME Action UK	Guideline	024	013	The point of the energy envelope is to manage overall energy expenditure - saying it "can be applied to all types of activity" implies a level of separation between different types of activity and misses the key aspect of the approach. Suggest changing this to "includes all types of energy expenditure"	Thank you for your comment. This has been edited to.' includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity'.

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ME Action UK	Guideline	024	014	We strongly agree with this statement, especially that overexertion can cause a worsening of symptoms	Thank you for your comment. Taking into account the stakeholder comments about lack of clarity this bullet point has been edited to,' helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise and or worsening their symptoms by exceeding their limits'
ME Action UK	Guideline	024	016	We strongly agree with this statement.	Thank you for your comment
ME Action UK	Guideline	024	018	We agree with this statement.	Thank you for your comment
ME Action UK	Guideline	024	021	This statement assumes that there will be periods where symptoms are improved, and then only suggests pulling back when symptoms are worse, not before they may get worse, despite another recommendation for pre-emptive rest. We do however agree that the approach should be flexible. Suggest changing this to "uses a flexible approach so that activity changes dependent on symptom severity, and reduces activity when symptoms are or may be about to get worse"	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse)'.
ME Action UK	Guideline	025	001	Again this bullet point assumes that increases in tolerance or activity are possible and to be aimed for. We are particularly concerned by the use of the word "tolerance" here. Instead change to "is a long-term approach that aims to reduce the chances of flares and relapses"	Thank you for your comment. After considering the stakeholder comments the committee agreed to keep the word tolerance to reflect that this guideline is directed at all people with ME/CFS. After considering the stakeholder comments recommendation 1.11.6 this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'
ME Action UK	Guideline	025	003	Despite significant evidence to the contrary, this statement of assumption still allows for the possible interpretation that ME/CFS could be caused by deconditioning. In evidence review G p335 line 50, the language used is "recognises that deconditioning is not the cause of ME/CFS."	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice

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				Why have the committee not used this more accurate language in the Guideline itself? We recommend changing this to: "recognises that deconditioning is not the cause of or a perpetuating factor of ME/CFS."	on maintaining and preventing the deterioration of physical functioning and mobility. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context
ME Action UK	Guideline	025	004	We agree that people with ME should be offered an assessment to develop an energy management plan with realistic expectations, however remain concerned about the language of "goals". Evidence Review G p336 line 26 states: "The committee noted that where goals are rigid and unrealistic this can result in false starts, flares and relapses. The committee commented on the findings in the qualitative evidence that people had felt pressured and blamed when they could not complete the programme even though it was making their symptoms worse. The committee acknowledged the controversy around the setting of fixed unrealistic goals and the importance of understanding realistic goal setting by both the person with ME/CFS and the healthcare professional supporting any programme." Where there is evidence of harm from goal setting, including relapses that "can lead to a long-term reduction in the person's energy envelope" (Guideline p44 line 29) there must be very strong evidence of benefit to recommend such a strategy even with the caveats of "realistic" attached. Such evidence is not presented in the evidence reviews. "and goals" should be removed from this sentence, and doing so would have no adverse impact on the Guideline or people with ME.	Thank you for your comment. As you note the committee discussed the use of goals and agreed that where they were included it was important that people should be supported to establish realistic expectations and develop goals that are meaningful to them. This is in line with the holistic personalised approach the guideline adopts. The committee acknowledge that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed and the committee have added a recommendation raising **awareness about** this in the flare up and relapse section of the guideline.
ME Action UK	Guideline	025	007	We agree with all of these bullet points	Thank you for your comment.

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ME Action UK	Guideline	025	012	Can this bullet point on rest and relaxation be linked to the specific recommendations around rest made at 1.11.23?	Thank you for your comment. This recommendation refers to the areas for assessment and this section is followed by recommendations on the symptom management for people with ME/CFS.. When writing guidelines there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	025	015	This implies that the management plan can be established by the healthcare professional alone, add in "work with the person to establish…"	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Work with the person to establish an individual activity pattern within their current energy limits that minimises their symptoms'.
ME Action UK	Guideline	025	018	We agree this should be a first step.	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
ME Action UK	Guideline	025	019	We strongly agree with the recommendation for pre-emptive rest.	Thank you for your comment.
ME Action UK	Guideline	025	021	While this may help some, we have heard from others that this can take more energy. We don't know of an evidence base for this, and cannot find one in the evidence reviews. We would suggest adding the word "consider" at the beginning of this bullet point to make it clear this may only be helpful for some.	Thank you for your comment. The recommendation is to work with the person to establish an individual activity pattern and these bullet points are examples of what might be useful. For this reason 'consider has not been added.
ME Action UK	Guideline	025	025	We strongly agree with this statement.	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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ME Action UK	Guideline	025	027	We strongly agree with this statement.	Thank you for your comment.
ME Action UK	Guideline	026	001	It is unclear if all three of these bullet points must be met, or if only one of them should be. However we agree that specialist and not generic services are required for people with ME.	Thank you for your comment. 'or' as has been added to each bullet point to clarify each situation is a reason for referral.
ME Action UK	Guideline	026	004	Physical activity advice from a specialist should be available to any person with ME who needs it, whether they are increasing or decreasing activity. As in other places in this Guideline, this sentence once again puts a focus on progressing physical activity, without a clear evidence base for doing so. Change this to: "Would like support in changing their physical activity pattern to match their current energy envelope".	Thank you for your comment. The committee recommended and described the expertise that should be available to a person with ME/CFS based on their needs in the multidisciplinary care section of the guideline (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care
ME Action UK	Guideline	026	006	This sentence again suggests that people with ME simply need to want to incorporate physical activity programmes into their life for it to be appropriate - without consideration for whether their current energy envelope would allow for this. During our community calls to discuss this draft Guideline, that were attended by over 70 participants, people expressed offence at this language. One participant told us that of course she "would like" to do physical activity, of course she "would like" to do new activities, of course she "would like" to return to her previous levels of health and fitness - but her energy envelope and ability to do these activities had nothing to do with what she	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. Then referral is to explore this possibility.

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				"would like". This was met with agreement from other participants. This sentence plays into tropes that people with ME simply need to undertake physical activity to recover, tropes that you have recognised to be problematic and inaccurate in the evidence reviews and supporting evidence. We very strongly urge the committee to remove all language suggesting people with ME simply need to "like" an activity programme, for it to be appropriate. Remove this sentence.	
ME Action UK	Guideline	026	009	We agree that more specialist advice is required for people with severe or very severe ME, but only where they would like it.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan.
ME Action UK	Guideline	026	014	"That changes in activity should be smaller and any increases (if possible) much slower." - Once again we see a focus on increases where the aim of energy management should be stabilisation and reduction of flares and relapses. Change this sentence to: "that changes in activity should be smaller (unless decreasing activity significantly to reduce symptom severity), and should focus on stabilisation and remaining within the person's energy envelope"	Thank you for your comment. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee included (if possible) to emphasise that any increases may not be possible and the plan should be developed by a physiotherapist or occupational therapist working in a ME/CFS specialist team.
ME Action UK	Guideline	026	016	We are pleased to see the inclusion of this section in the Guideline.	Thank you for your comment. The committee agree and ,

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				It is important to recognise the impact ME can have on general health, and work to mitigate that in ways that recognise the harm of overexertion itself. However it seems important that an additional recommendation is added to this section - in our experience, it is common that people will search for and read just the part of a Guideline that is relevant to them on that particular day. When read alone this section implies that normal management advice relating to muscle strength and other areas could be appropriate. We strongly agree with the definition of physical maintenance laid out on page 44. Incorporating all or part of this here would make it significantly clearer what the aim of physical maintenance is. We particularly note the helpful and clarifying statement on page 44 line 15 that states: "Such activity is undertaken within the person's energy envelope and avoids pushing through boundaries of tolerance." We therefore strongly urge the committee to at least add a statement that says: "Be aware that any activity undertaken as part of physical maintenance should be within the person's energy envelope and should avoid pushing through the boundaries of tolerance. Consider the person's other activities of daily living when giving advice." Bringing this important aspect in from the definition of physical maintenance will ensure this recommendation is in line with other advice and doesn't harm people with ME by generalised and inappropriate advice being given.	'Include strategies to maintain and prevent deterioration of physical functioning and mobility in the care and support plans for people with ME/CFS. Strategies may need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the care and support plan and the priorities and symptoms that people may have.
ME Action UK	Guideline	026	022	We would recommend the removal of the word endurance here. In healthy people, increasing endurance is generally achieved by	Thank you for your comment. 'Strength and endurance' has been edited to 'muscle function'.

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				repeatedly exceeding one's capacity - something this committee has explicitly warned can cause PEM/PESE and relapses for people with ME.	
ME Action UK	Guideline	027	021 - 023	Remove the word "unstructured". The evidence reviews provide significant evidence that structured exercise (as in the form of graded exercise therapy) is in fact also harmful. There is also a double negative in the sentence that leads to confusion. People with ME clearly should not be advised to take part in unstructured exercise even as part of a supervised programme. We suggest rewording this sentence to: "Do not advise people with ME to undertake generalised exercise, such as telling them to go to the gym or exercise more, because this may worsen their symptoms"	Thank you for your comment. After considering the stakeholder comments this has been edited to, 'do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.'
ME Action UK	Guideline	027	003	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	027	08	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	027	014	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	027	020	We support the inclusion of a section on physical activity, due to the significant reports of harm from programmes relating to physical activity in the evidence reviewed, and our personal experience of such therapies and programmes. Considering the harm caused by past recommendations, and that other sections of this Guideline make clear statements not to offer medicines, CBT or anything else as a treatment or cure for ME, we see it as equally if not more important that this is reiterated here. Add a sentence: "Be aware that physical activity and/or exercise is not a treatment of cure for ME, and may worsen their symptoms."	Thank you for your comment. *Treatment or cure* To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. The recommendation above this one is clear that programmes not overseen by a ME/CFS specialist team may worsen symptoms.

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ME Action UK	Guideline	027	024	This is a very helpful addition that we strongly agree with overall. Thank you to the committee for taking the reports of harm seriously, and actively following the evidence base.	Thank you for your comment.
ME Action UK	Guideline	028	012 - 014	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: Why has the committee chosen to call this a programme? Programme is defined in Oxford Dictionaries as "a set of related measures or activities with a particular long-term aim." To us, this has connotations of expected change, yet that very clearly cannot be guaranteed. The committee could choose language without connotations of expected change and ultimately improvement, such as "Physical Activity Advice", Physical Activity Support" or a "Physical Activity Plan". Why the difference here between an Energy Management *Plan* and a Physical Activity *Programme*? We very strongly urge the committee move away from the language of a programme.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Programme* The programme is part of the care and support plan and the energy management plan, 'programme' is used to illustrate it is addresses physical activity or exercise in particular.

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ME Action UK	Guideline	028	001	We strongly agree with this bullet point, and consider it an important part of the overall Guideline.	Thank you for your comment
ME Action UK	Guideline	028	003	We strongly agree with this bullet point, but the use later on of the term "physical activity programme" for people with ME makes this less clear. We suggest keeping this bullet point as is, but changing the language of "physical activity programme" used later in this Guideline. We will make a separate comment about this.	Thank you for your comment The programme is part of the care and support plan and the energy management plan, 'programme' is used later to illustrate it is addresses physical activity or exercise in particular.
ME Action UK	Guideline	028	006	This recommendation is a necessary and clear repudiation of a paradigm that has caused very significant harm. As you have found in the evidence reviews, trials commonly did not measure adverse events, outcomes were switched and the quality of evidence was almost entirely very low. Yet data from surveys of many thousands of patients demonstrated significant harm from such approaches. It is vital that this committee have taken into account the grey literature on these areas, and we urge them to retain this statement. We would change just one thing in this sentence - removing the word fixed. According to Oxford Languages, the definition of incremental is "relating to or denoting an increase or addition, especially one of a series on a fixed scale". This language of "incremental increases" already covers what is necessary here, without the additional qualifier of 'fixed'. Incremental increases have been the core part of activity programmes provided to people with ME in the past, however the terminology of fixed has not previously been used. In the 2007 CFS/ME Guideline, it states: "People with mild or moderate CFS/ME should be offered GET that includes planned increases in the duration of physical activity. The intensity should then be increased when appropriate..." The Guideline also states: "Encourage them to undertake this exercise for at least 5 days out of 7, or build up to this level if and when possible."	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes

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				Language was already included that allowed for some level of flexibility in increasing exercise, yet it is under this Guideline that so much damage has been caused. The Oxford Brookes Survey Report (2019), which specified therapy must have been received since 2007 as an inclusion criteria, demonstrates that over two thirds of respondents who underwent this therapy whilst the 2007 Guideline was in place deteriorated. Further survey data support this finding. It is quite clearly not only "fixed" incremental increases in activity that have caused harm, but an approach that's basis is any type of incremental increases. We do not wish to take away from the incredible step that a recommendation against graded exercise therapy is for the wider community, but do urge the committee to remove the word "fixed" from this sentence.	of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
ME Action UK	Guideline	028	008	While we strongly agree with the sentence, it could be better said as "activity or exercise programmes as a cure or treatment for ME, including any programmes based on deconditioning as a cause or perpetuating factor of ME."	Thank you for your comment. After considering the range of stakeholder comments, this recommendation has been edited to,' Do not offer people with ME/CFS …. physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories' *as the cause of* has been deleted.

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ME Action UK	Guideline	028	010	We very strongly agree with this recommendation, in particular the recommendation against using the Lightning Process, that has no evidence base and draws on techniques, such as activities outside the person's energy envelope, that are contraindicated for people with ME. In #MEAction UK's community calls to discuss this draft Guideline, and in emails we've received, some people with ME have raised concerns about osteopathy being included alongside life coaching, neurolinguistic programming, and the Lightning Process, and so we wished to pass this along to the committee. It is unclear if this recommendation means therapies derived from *combinations of* osteopathy, life coaching and neurolinguistic programming, or each of these sources alone.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)
ME Action UK	Guideline	028	012	In the 2007 Guideline advice was given for people with ME to increase their activity and exercise, this included sentences such as "People with mild or moderate CFS/ME should be offered GET that includes planned increases in the duration of physical activity. The intensity should then be increased when appropriate..." and "Encourage them to undertake this exercise for at least 5 days out of 7, or build up to this level if and when possible." In spite of language that includes qualifiers of "when appropriate" and "if and when possible" many people with ME have been harmed by these recommendations. It is clear the committee has understood and recognised the extensive harm caused, and there is very significant relief that the lived experience of so many people has not been ignored. This recommendation for physical activity programmes, while adding more qualifiers than the 2007 Guideline, appears likely to lead to the same outcomes of harm, deterioration, resultant	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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				distrust in healthcare professionals and therefore worse overall care for people with ME. It is right that people with ME, alongside those with other debilitating illnesses, have access to specialist support around physical activity when requested, especially as this aspect appears key in preventing relapses. However, in their recommendation of "physical activity programmes" the committee appear to have made up an entirely new management approach that is not backed by the evidence base, be that research literature or qualitative data. The committee has acknowledged that graded exercise therapy has done harm, and has explicitly recommended against this. Under 'Other Exercise Interventions' (Evidence review G, page 154-165), not a single outcome rates higher than 'very low' on the quality of evidence, nor has any qualitative evidence been identified. We therefore strongly question why the committee has created a newly defined 'physical activity programme' in the Guideline. Our strong recommendation here is to remove this non-evidence based 'programme' from the Guideline in its entirety, and instead provide greater access to specialist advice and support on energy management, as this should include support in managing fluctuations in a person's energy envelope anyway. This would enable access to physical activity advice for all people with ME, and not just those who "are ready" or "would like" to "progress their physical activity".	interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
ME Action UK	Guideline	028	014	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people

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				In case the committee does not take this step, here are our further comments: Evidence Review G p336 line 44 states: It was the opinion of the committee that a physical activity or exercise programme can be beneficial for people who have chronic fatigue (not ME) and in a subset of people with ME who have already begun to improve and feel they want to do more." (Our bolding) Despite this, the Guideline says "Only consider a physical activity programme for people with ME/CFS who are ready to progress their physical activity beyond their current activities of daily living, or would like to incorporate physical activity into the management of their ME/CFS." This difference between "and" and "or" here is vital. By defining the prerequisite for undertaking this newly defined programme as something a person simply would like to do, instead of also being ready to do, it opens up the possibility for significant harm. We very strongly request that "or" is changed to "and" in this sentence.	with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
ME Action UK	Guideline	028	017	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: It is under the purview of health professionals trained in ME that such significant harm has occurred and at present this recommendation does not go far enough to support the paradigm shift needed to halt the harm.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by

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				We recommend adding: "by a physiotherapist or occupational therapist with training and expertise in ME as per this Guideline." The shift required will mean many practitioners who wish to stay working in healthcare relating to ME retraining per this Guideline. It is simple enough for the committee to make this clear.	physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
ME Action UK	Guideline	028	020	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: Qualitative evidence quite clearly demonstrates that most people with ME deteriorate following graded exercise therapy, furthermore Evidence Review G acknowledges that most clinical trials did not record harm from this therapy. Taking this into account, we find it perplexing that the committee has recommended to "Explain that some people with ME/CFS have found that physical activity programmes can make their symptoms worsen, for some people it makes no difference and others find them helpful." (Our bolding) It would be more accurate to write that "many" or "most" people with ME have found the physical activity programmes can make their symptoms worsen.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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					interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The committee agreed not to change some to many, this point was to illustrate that the impact of a physical activity or exercise programme can vary.
ME Action UK	Guideline	028	023	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: Again, we disagree with the terminology of "programme" here. We agree that physical activity should be personalised.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the

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					review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Programme* The programme is part of the care and support plan and the energy management plan, 'programme' is used to illustrate it is addresses physical activity or exercise in particular.
ME Action UK	Guideline	028	025	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: We agree that not worsening symptoms should be the highest priority. The committee could make this clearer by adding a first bullet point that simply states: "should not worsen symptoms". If advice or a programme is worsening symptoms, it is not fit for purpose, yet for the past 13 years this has been considered acceptable. We urge the committee to take a very clear stance that this is not acceptable.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D),

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					multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
ME Action UK	Guideline	028	027	We recommend that this non-evidenced based and newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: We agree that any physical activity should remain inside the person's energy envelope, unfortunately this bullet point suggests that this only needs to happen at the start. The Guideline does state that any increases should be within the energy envelope later, but this is a key principle that must not be understated. The committee could make this clearer by stating that any physical activity programme should "start by reducing the person's activity to within their energy envelope and stay within their energy envelope throughout".	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Energy envelope*

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					The following bullet point includes that people should stay within their energy limits. This is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly. To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
ME Action UK	Guideline	028	028	We recommend that this non-evidenced based and newly defined physical activity programme be removed from the Guideline. In case the committee does not take this step, here are our further comments: The Guideline recognises that the person with ME/CFS is the "best judge of their own limits" (page 24, line 17). Surely this should be considered in this bullet point, beyond just that ability to maintain their baseline activities. If the person judges that they have not yet reached their limit, then minor increases may be appropriate, however if the person feels they are at their limit, or that they have other life events ahead that require energy expenditure, this must be taken into account - decreases in physical activity may be just as appropriate as increases dependent on circumstances. This is recognised in Evidence Review G p336 line 25 where it says "Another finding highlighted the need for programmes to fit into their lives accounting for essential life activities."	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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				We recommend changing this bullet point to: "Adapt to changes in circumstance or the person's energy envelope by decreasing or increasing activity as appropriate."	interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The committee note this is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly.
ME Action UK	Guideline	029	001	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: "Use flexible increments" - albeit slightly different language, this is ultimately what the 2007 CFS/ME Guideline also advised, and is what has caused such harm. Increments implies additions or increases. However this will not be appropriate for all people. We question why the committee has decided to focus so strongly on increments instead of words such as "changes" that encompass the wider range of possibilities people with ME confront in living with this chronic condition. The focus of "want to improve their physical abilities" is yet again deeply offensive to the majority who are too ill to do this, as if wanting to is the only barrier.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The

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				We urge the committee to remove this bullet point. It has no place in ME care.	committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). After considering the stakeholder comments the committee edited this bullet point to, 'making flexible adjustments to their physical activity (up or down as needed) to help them gradually improve their physical abilities while staying within their energy limits'.
ME Action UK	Guideline	029	003	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: We agree that recognising flares or relapses early is important. It would be helpful if such terms were defined at the beginning of the Guideline instead of the end, as the nuanced difference is currently lost. We also agree that outlining how to manage a flare or relapse is important. It would be helpful for the committee to recommend that this outline should be defined before the flare or relapse occurs. Simply adding the bold words to the recommendation: "recognise a flare or relapse early and outline how to manage it before it occurs…" would help make sure any advice incorporated this.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the

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					review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Flare-ups and relapse* This bullet point in the previous recommendation refers to what should be in the plan and this is before the plan is implemented and includes recognising a flare-up or relapse early and outlining how to manage it. The format of NICE guidelines has the definitions at the end of the recommendations.
ME Action UK	Guideline	029	005	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: We agree that regular reviews are important, but would add that the professionals should record any flares or relapses that have taken place. We therefore suggest the bullet point is changed to include the part in bold: "incorporate regular reviews and record any flares or relapses."	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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					interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The recommendations in this section include that the programme should be reviewed regularly.
ME Action UK	Guideline	029	006	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: This recommendation could be suggesting that agreement on how to manage flares or relapses is considered once the person is in a flare or relapse. This is too late. Change to: "Agree with the person in advance how to adjust their physical activity after a flare or relapse."	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and

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					Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Flare-ups and relapse* The bullet point in the previous recommendation refers to what should be in the plan and this is before the plan is implemented and includes recognising a flare-up or relapse early and outlining how to manage it.
ME Action UK	Guideline	029	009	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: On page 28 the Guideline recommends "a physiotherapist or occupational therapist with training and expertise in ME/CFS" should be involved in physical activity advice. However this recommendation now mentions a specialist physiotherapy service. Is this service relating to flares and relapses intended to be different from the support given in the initial stages of considering physical activity with the person with ME? Why is occupational therapy mentioned previously but not here? Should the person contact this service instead of their named contact as per recommendation 1.10.3 that also mentions support during a relapse?	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and

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					Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The committee agreed that for people with ME/CFS it was important that the healthcare professionals with the appropriate clinical background and training supported any physical activity plans, here referral is to physiotherapist or occupational therapists and then it is the physiotherapist that oversees a physical activity programme, as such the appropriate professional to access for support if needed during a flare up or relapse.
ME Action UK	Guideline	029	010	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: We agree that reducing activity is vital during a flare or relapse.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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					interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
ME Action UK	Guideline	029	012	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: There must be a bullet point making clear that avoiding another flare or relapse is the highest priority. There is also concern that "establishing a new physical activity baseline" doesn't explain that this should be reduced, nor that cycles of physical activity and flare are more likely to lead to relapse. We would therefore recommend replacing this bullet point with: "identifying what may have caused the flare or relapse and changing physical activity levels to prevent this in future." Continuing with physical activity programmes after flares or relapses have occurred should ideally be advised against and, if undertaken, the risks of further flares or relapses should be clearly discussed. While this sentence should be replaced, the use of the word "and" is an important qualifier that should not be changed if the committee decides to keep such a sentence: "only once symptoms stabilise and the person feels able to resume physical activity, …"	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).

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					Flare-ups and relapse The collaborative personalised programme includes recognising a flare-up or relapse early and outlining how to manage it, as part of this any strategies would be individual and agreed with the person with ME/CFS.
ME Action UK	Guideline	029	014	We recommend that this non-evidenced based and entirely newly defined physical activity programme is removed from the Guideline. In case the committee does not take this step, here are our further comments: This recommendation appears confused. In the section "Terms used in this Guideline" a flare is defined as transient, and typically resolves after a few days. Yet this recommendation says "Advise people with ME/CFS after a flare that the time it takes to return to the level of physical activity they had before the flare varies from person to person." We actually believe this is more accurate than the 1-3 days timeline proposed in the "Terms used in this Guideline" however note that for some people they may never return to the level of physical activity they had before the flare - in this case it should be considered a relapse, and the person with ME should also be advised of this as a possible outcome. Change this recommendation to: "Advise people with ME/CFS that the time it takes to return to the level of physical activity they had before a flare varies from person to person, and that when a flare develops into a relapse this can lead to a long-term reduction in the person's energy envelope."	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Flare-ups and relapse*

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					The collaborative personalised programme includes recognising a flare-up or relapse early and outlining how to manage it.
ME Action UK	Guideline	029	017	We recommend the addition of a referral to a sleep clinic in cases where other approaches do not help. A sleep clinic can determine whether the person has additional problems such as sleep apnoea and recommend appropriate treatments.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS and have included a recommendation on referral to an appropriate specialist if the personalised sleep management strategies do not result in improvement.
ME Action UK	Guideline	029	018	This section should further explain the role of rest, and discuss interventions for more severe sleep issues, providing specific advice for people with ME including pharmaceutical interventions.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
ME Action UK	Guideline	029	019	The word 'sleep' should be added to this sentence alongside the word 'rest'. Daytime sleep is discouraged by clinics at the moment but is often vital for energy management.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.

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ME Action UK	Guideline	029	020	We strongly agree that rest periods are a part of all management strategies for ME and are pleased the committee has made such a clear statement on this.	Thank you for your comment.
ME Action UK	Guideline	030	003	An additional research recommendation on treatment of orthostatic intolerance in people with ME should be made, due to the paucity of evidence here. Further training in testing and interventions for orthostatic intolerance for healthcare professionals treating people with ME should also be required.	Thank you for your comment. Research recommendations can only be made where the evidence has been searched for within the guideline. The treatment of orthostatic intolerance was not included in the scope of this guideline as a topic to consider, and therefore the committee were unable to make research recommendations on this topic.
ME Action UK	Guideline	030	004	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	030	010	We agree that people should be referred to secondary care for orthostatic intolerance if the professional treating ME is not trained in orthostatic intolerance.	Thank you for your comment.
ME Action UK	Guideline	030	010	We strongly agree with the recommendation to follow advice on neuropathic pain in adults, and not the new Guideline on chronic pain in adults that recommends treatments contraindicated in ME.	Thank you for your comment.
ME Action UK	Guideline	030	010	We agree that the NICE guidance on headaches should be referred to.	Thank you for your comment.
ME Action UK	Guideline	031	002	Nausea could be caused by a variety of factors, including comorbid conditions. The origin of the nausea should be investigated and addressed accordingly. We recommend this section be edited accordingly.	Thank you for your comment. This recommendation refers to general strategies to minimise nausea and not investigation of nausea. The following recommendation has examples of when people should be referred for a dietetic assessment.
ME Action UK	Guideline	031	002	There are specific anti-nausea medications. A general reference to them should be included here. We recommend the following be added at 1.11.28: "Where nausea is not remedied by fluid intake and eating habits:	Thank you for your comment. No evidence was identified to support the committee making recommendations on nausea and they agreed to make this general consensus recommendation on strategies however they agreed they were unable to make any recommendations for

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				● Consider standard antiemetics Consider revisiting the energy management plan as nausea may be induced by over-exertion"	specific medications. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
ME Action UK	Guideline	031	006	Evidence review F makes a much clearer statement on the use of medicines for symptom management than is given here: "The committee acknowledged that while there are not any current pharmacological treatments or cures for ME/CFS, people with ME/CFS have found some drugs when used appropriately with advice and support from health care professionals can be helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis." (p94 line 30) We urge the committee to include a recommendation in line with these remarks, that where a physician or person with ME believes that a medicine may provide symptomatic relief, their GP should offer advice and support, and prescribe it if in their judgement there is potential benefit with low risk for harm. Some over-the-counter interventions may mitigate symptoms despite not treating or curing the root cause(s) of ME. We recommend that use of low-risk, low-cost interventions be supported in the Guideline if the doctor and person with ME agree. Add a recommendation: "Be aware that some medicines or supplements can be helpful in managing the symptoms of ME and should be discussed and prescribed on an individual basis."	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. As you note the discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

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ME Action UK	Guideline	031	017	We would like the word "paediatrician" to be replaced by "paediatrician with training in accordance with this Guideline and experience of ME." It is vital that all those involved in the prescribing of care for people with ME, and especially children and young people, have an understanding of ME based upon this Guideline.	Thank you for your comment. After considering the stakeholder comments the committee agreed to change paediatrician to medical professional trained and experienced in in paediatric prescribing. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	032	001	We would like to see a recognition that many people experiment with diet to try and gain some relief from symptoms. As with medication and supplements, we would like to see a recommendation that healthcare professionals take a supportive attitude, advising on potential harms and benefits if they are qualified, or referring the person to a dietician if not.	Thank you for your comment. Dietary assessment, including the use of restrictive and alternative diets, is included in the assessment and care planning recommendations. Discussion about the diets that people follow would be part of this assessment and in reviews of their care and support plan. In addition, the committee recommend referral to a dietician with a special interest in ME/CFS for people with ME/CFS who have a restrictive diet.
ME Action UK	Guideline	032	008	Some people with ME experience weight gain rather than loss. We recommend this be taken into account for this section of the Guideline. Many people find that excluding certain foods can help reduce symptoms. We recommend the following to be added to the end of this sentence: ".. or wish to try excluding certain foods from their diet".	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in

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					ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.
ME Action UK	Guideline	032	011	We agree with this recommendation, including reference to those who are predominantly housebound or bedbound.	Thank you for your comment.
ME Action UK	Guideline	032	015	We recommend the following wording to be added to this recommendation: "Where a person wishes to try vitamin or mineral supplements, be supportive but advise on safe limits and any possible harms or side effects."	Thank you for your comment. This recommendation has been slightly reworded to indicate that if people choose to take a vitamin or supplement the potential side effects of taking higher doses should be explained.
ME Action UK	Guideline	032	021	We agree with this recommendation, however would add to the end "and has training in accordance with this Guideline."	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation. To note this recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.

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ME Action UK	Guideline	033	004	We agree with this recommendation, however would add to the end "and has training in accordance with this Guideline."	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. To note this recommendation has been reworded to describe paediatric dietician as a 'paediatric dietician who has a special interest in ME/CFS', the committee recognised that currently paediatric dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are paediatric dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.
ME Action UK	Guideline	033	006	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	033	015	We agree with this recommendation, and all the bullet points, especially the reference to possible "oral nutrition support and enteral feeding".	Thank you for your comment.
ME Action UK	Guideline	034	001 - General	While we agree that people with ME may need psychological support and should have access to this, we argue below that the focus on CBT alone in this guideline is not evidence based and will lead to less access to support than is desirable and necessary. We recommend changing the title of this section to just "Psychological support", and creating recommendations that cover all therapies people with ME may receive for psychological support. Looking through Evidence Review H - we note that out of 161 outcomes of CBT that were assessed, 113(70.2%) had a rating of very serious risk of bias and the remaining 48(29.8%) had a serious risk of bias. The vast majority (143/88.8%) received a quality rating of very low, with the remaining outcomes (18/11.2%) receiving a quality rating of low.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). After considering the range of stakeholder comments the committee edited the title of this section to remove psychological support recognising this only referred to CBT.

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				In looking at Evidence Review H, Appendix J we also note that the minimal important difference (MID) used throughout appears to have been 0.5xSD. We cannot find any analysis of a minimal important difference of one standard deviation, but considering the inconsistent results we believe using a slightly higher MID would have led to every or almost every outcome being considered not clinically important. In the overall summary in Evidence Review G for cognitive behavioural therapy the committee found that "most of the clinical evidence showed no clinical difference" (p323 line 28) and that where they did find "evidence of benefit [this] was not consistent" (p325 line 42). The committee discussed that there was a "lack of clarity over the intervention components" (p325 line 48) and that "harms [...] were rarely included as an outcome and reported" (p326 line 6). Overall they concluded that various factors meant it was "difficult to make confident conclusions about the evidence." (p326 line 5) The committee goes on to note that CBT "is one type of supportive psychological therapy which aims to improve wellbeing and quality of life" (p326 line 11 - emphasis added). Yet in the next sentence note that "benefits to quality of life and psychological status were not demonstrated in the clinical effectiveness evidence." (p326 line 14) Despite this lack of evidence, "[t]he committee agreed that CBT has a role in helping to manage the psychological effects of a chronic illness such as ME/CFS and can be particularly helpful for improving 'secondary disability' such as sleep, depression, and dietary issues" (p326 line 20) - yet we then see that no outcomes on dietary issues were assessed, and "[m]ost of the evidence showed no clinical difference compared to usual care	*CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *MIDs* The MIDs are agreed by the committee at the protocol stage and they agreed in the absence of any published and accepted MIDs to use the default MIDs proposed by the GRADE working group (see the methods chapter for more detail.)

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				or waiting list for [...] psychological status [...] and sleep quality." (p323 line 28) The aspects of CBT that were apparently more helpful included: ● "[t]hemes of validation, relationship with the therapist, individualised care, self-management support and ongoing support" (p342 line 41) ● providing support for people (p325 line 3) ● "The simple act of talking to someone was of benefit" (p325 line 5) ● "people were comforted by the knowledge that the therapist was available if they needed help" (p325 line 6) ● With the last two findings being "closely related to the theme of the relationship with the therapist and likely to be dependent on the establishment of a good therapeutic relationship" (p325 line 8) ● "Benefits of tailored care to people with ME/CFS" (p327 line 16) Each of these aspects are "common across other interventions" (p324 line 42). In discussing other psychological/behavioural interventions the committee found three findings in which they had moderate confidence: "There was moderate confidence in the finding that learning about the diagnosis, symptoms, possible causes and prognosis increased understanding and confidence in adults who had experienced education/information interventions. There was moderate confidence in the finding that an evidence-based source of information was welcomed due to issues with identifying reliable information on the internet and some felt more able to assess information about the illness and treatments more critically. There was moderate confidence in the finding that	

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				some people realised that they had to focus on acceptance and coping with the illness rather than curing it." (p330 line 8) These aspects are common to generalised support that we strongly believe every person with ME/CFS should have access to. Looking beyond ME to other chronic or long-term illnesses, where there is also a need to support some patients in dealing with the impact of their symptoms and living with their illness, there is at least some evidence that psychological interventions other than CBT can produce positive outcomes for patients. There is also support within that evidence for tailored psychological interventions, which may utilise different formats, durations and facilitators, recommended based on the person's illness and symptoms. For example, a randomised control trial (RTC) published in 'The Oncologist' looked at the one-year effect of a nurse-led psychosocial intervention on depressive symptoms in patients with head and neck cancer[1], and found that levels of depressive symptoms were significantly lower in the intervention group. The authors note that "several meta-analyses and reviews have shown that psychosocial interventions are effective in diminishing depressive symptoms in the general cancer population... [but that] There is no evidence that one intervention is superior to another." Similarly, a rapid systematic review of RTCs published in BMC Psychology looked at the effectiveness of psychological interventions to improve quality of life in people with various long-term conditions,[2] reviewing studies encompassing a variety of psychological interventions, and found promising results for utilising psychological interventions to improve quality of life for patients with long-term conditions. The authors noted the	

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				importance of “actively involving patients in their care and tailoring [...] interventions to patients’ needs”. Other studies have been conducted into the utility of different psychological interventions in various long-term conditions, including: a randomised clinical trial finding positive results from caregiver-assisted coping skills training in lung cancer patients[3]; a systematic review of psychological interventions for adolescents and young adults living with chronic illness[4]; and a Cochrane Review of psychological interventions for coronary heart disease [5]. We strongly support people with ME receiving the support they want and require to adapt to this devastating illness, including the psychological support that has ironically long been denied them through “inappropriately delivered” CBT (p326 line 27). By elevating CBT as the only therapy recommended this perpetuates the idea that people with ME necessarily need to manage their thinking and behaviour in order to manage their symptoms, in contradiction with the evidence laid out above. Based upon the evidence presented by the committee and additional evidence of psychological support and therapies in other physical illnesses, we can only conclude that this section should be rewritten A more general recommendation should be made to consider and discuss with the patient whether psychological support might be helpful - CBT could be included as one of many therapies. This section on psychological support could then lay out factors that would apply to any psychological support delivered to people with ME. It should recommend that all psychological support be given by a professional with training in accordance with this Guideline, and experience of ME. General pointers relating to	

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				what the therapy should and shouldn't include would then address all the types of therapy people with ME might seek out and receive, meaning that even private therapists would have a resource to turn to. This could retain the excellent recommendations this committee has made, such as: ● Psychological therapy "should be only delivered by a healthcare professional with appropriate training and experience in-[...] ME/CFS, and under the clinical supervision of someone with expertise in [...] ME/CFS." (Guideline p34 line 6) ● Psychological support "is not curative" (Guideline p34 line 12) ● "takes a non-judgemental, supportive approach to the person's experience of symptoms and the challenges these present" (Guideline p34 line 19) ● "developing a shared understanding with the person about the main difficulties and challenges they face" (Guideline p35 line 1) ● Regular review (Guideline p35 line 9) ● "Involve parents or carers in the therapy wherever possible" (Guideline p35 line 19) ● "adapt therapy to the child or young person's cognitive and emotional stage of development" (Guideline p35 line 20) This approach could provide people with ME who want psychological support with the guidance they deserve, without "pigeonholing" them into an approach that can never be one-size-fits all. 1. van der Meulen IC, May AM, Ros WJ, Oosterom M, Hordijk GJ, Koole R, de Leeuw JR. One-year effect of a nurse-led psychosocial intervention on depressive	

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				symptoms in patients with head and neck cancer: a randomized controlled trial. Oncologist. 2013;18(3):336-44. doi: 10.1634/theoncologist.2012-0299. Epub 2013 Feb 21. PMID: 23429740; PMCID: PMC3607532. 2. Anderson N, Ozakinci G. Effectiveness of psychological interventions to improve quality of life in people with long-term conditions: rapid systematic review of randomised controlled trials. BMC Psychol. 2018;6(1):11. Published 2018 Mar 27. doi:10.1186/s40359-018-0225-4 3. Porter LS, Keefe FJ, Garst J, et al. Caregiver-assisted coping skills training for lung cancer: results of a randomized clinical trial. J Pain Symptom Manage. 2011;41(1):1-13. doi:10.1016/j.jpainsymman.2010.04.014 4. Sansom-Daly, U. M., Peate, M., Wakefield, C. E., Bryant, R. A., & Cohn, R. J. (2012). A systematic review of psychological interventions for adolescents and young adults living with chronic illness. Health Psychology, 31(3), 380–393. https://doi.org/10.1037/a0025977 5. Richards SH, Anderson L, Jenkinson CE, Whalley B, Rees K, Davies P, Bennett P, Liu Z, West R, Thompson DR, Taylor RS. Psychological interventions for coronary heart disease. Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD002902. DOI: 10.1002/14651858.CD002902.pub4. Accessed 12 December 2020.	
ME Action UK	Guideline	034	025 - 027	The phrase "to work towards meaningful goals" is very problematic. It implies that ME sufferers can control improvement over time, when this is not supported by the evidence presented. We would suggest, after 'help the person to', substituting with '..adapt to living with long-term illness'.	Thank you for your comment. The bullet point above explains that CBT is a collaborative, structured, time-limited intervention that focuses on the difficulties people are having at that time. The strategies and goals are directed by the person with ME/CFS. The next recommendation includes reviewing their plan regularly to see if

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					their self-management strategies need to be adapted, for example if their symptoms or functioning change. The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
ME Action UK	Guideline	034	002	As we understand it, NICE has two levels of recommendation - "offering" and "considering". Based on the fact that 88.8% of outcomes of CBT assessed received a quality grade of very low, and the remaining 11.2% received a grade of low, there can be no justification for the committee recommending this at the "offer" level, even within the given qualifiers. If this recommendation remains it must be downgraded to the "consider" level. Furthermore the evidence does not support the recommendation of CBT for "people with ME/CFS who would like to use it to support them in managing their symptoms." Evidence review G p323 line 28 clearly states: "Most of the evidence showed no clinical difference compared to usual care or waiting list for quality of life, cognitive function, physical function, psychological status, pain and sleep quality."	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of

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				The only evidence of benefit in symptom presentation was highly inconsistent, with some studies showing a benefit and others no clinical difference, and based upon "general symptom scales". Furthermore "evidence was not stratified by diagnostic criteria used, so theoretically, studies including potentially different populations could have been combined." - this is of particular concern in a disease defined by its symptoms, and once again undermines the effectiveness of CBT when there is no clinical difference for the actual symptoms of ME that were individually assessed: cognitive difficulties, unrefreshing sleep, and pain. Finally, in grading the quality of evidence every single CBT outcome was rated as having serious or very serious population indirectness, as PEM was not a mandatory symptom for inclusion (Evidence Review H). The importance of this cannot be understated when considering evidence of symptom benefit, and most of the studies can, therefore, be discounted. The focus on symptom management in this recommendation is consequently in contradiction of the evidence. Even a focus on psychological distress is non-evidence based here. We cannot conclude anything other than that CBT should not be recommended as clinically and cost effective in this Guideline. However if the committee do decide to retain CBT we must urge them to change this recommendation to: "Only consider cognitive behavioural therapy (CBT) for people with ME/CFS who would like to use it to ~~support them in managing their symptoms of ME/CFS and to~~ reduce the psychological distress associated with having a chronic illness. Do not offer CBT as a treatment or cure for ME/CFS."	the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. In addition recommendation 1.12.29 has been edited to clarify that CBT aims to improve quality of life, including functioning,

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					and to reduce the distress associated with having a chronic illness.
ME Action UK	Guideline	034	006	As noted in the Evidence Review G there was a "lack of clarity over the intervention components" (p325 line 48) and a "potential for harm when inappropriately delivered" (p326 line 27). Considering this potential for harm, the low and very low quality of evidence, and the commonality of the positive aspects of CBT with other psychological therapies, we conclude that experience in CBT for ME/CFS is not the issue here, but access to generalised psychological support is. We therefore, again recommend that the committee recommends access to psychological support tailored to the person with ME, without making a recommendation of CBT over other modalities. If the committee decides to retain the recommendation for CBT, it must make absolutely clear that training must be in accordance with this Guideline, to safeguard against further harm from inappropriate delivery. See edit in bold below: "CBT should be only delivered by a healthcare professional with appropriate training in accordance with this Guideline and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS."	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
ME Action UK	Guideline	034	011	Evidence Review G p325 line 22 states: "Regarding the effect of CBT on symptom improvement, the response in adults was mixed, with some reporting a gradual improvement which did not reach a premorbid level of functioning, some reporting no change and some reporting a worsening of symptoms." However a	Thank you for your comment. It is good practice to discuss the risks and benefits of any intervention and CBT is no exception. This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and

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				recommendation that simply advises to "discuss… the potential benefits and risks" falls far short of this detailed information which is needed to enable people with ME to make informed decisions and consent to this therapy. As with physical activity, there must be a clear acknowledgement of each of these outcomes. Recommendation 1.11.19 states: "Tell people about the risks and benefits of a physical activity programme. Explain that some people with ME/CFS have found that physical activity programmes can make their symptoms worsen, for some people it makes no difference and others find them helpful." We strongly urge the committee to include an equivalent statement on CBT - e.g. "Tell people about the risks and benefits of cognitive behavioural therapy. Explain that some people with ME/CFS have found that cognitive behavioural therapy can make their symptoms worsen, for some people it makes no difference and others find it helpful." Any recommendation of CBT should come with the caveat that it may be counterproductive and harmful for some sufferers, particularly those in the severe or very severe category but also those in the moderate and mild categories. The exertion required to talk, think and attend sessions, even online sessions, may lead to a worsening of symptoms.	experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks for the person and able to ensure the person with ME/CFS makes an informed choice.
ME Action UK	Guideline	034	012	This is an important inclusion that we agree must be mentioned when discussing whether the person with ME/CFS should consider CBT.	Thank you for your comment. After considering the stakeholder comments, this has been deleted here but included at the beginning of the first recommendation.
ME Action UK	Guideline	034	013	Evidence Review G (p326 line 14) states: "benefits to quality of life and psychological status were not demonstrated in the clinical effectiveness evidence."	Thank you for your comment. In the cost effectiveness review quality of life gains were demonstrated.

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				There is a serious problem when a therapy is "designed to improve wellbeing and quality of life" as this bullet point states, yet there is no clinical effectiveness evidence to suggest this outcome actually occurs. Remove this bullet point.	*Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to

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					accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
ME Action UK	Guideline	034	014	The phrase 'aims to improve functioning' is not evidence based in the context of ME/CFS. Evidence Review G (p323 line 28) states: "Most of the evidence showed no clinical difference compared to usual care or waiting list for… physical function". In keeping this "aim" the committee sets people with ME/CFS up to fail. We urge them in the strongest way possible to remove the first limb of this bullet point, leaving: "aims to reduce the psychological distress associated with having a chronic illness."	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
ME Action UK	Guideline	034	016	We strongly urge the committee to reword this bullet point to "recognises that 'abnormal' illness beliefs and behaviours are not an underlying cause of ME/CFS" The second limb of this bullet point directly undermines the first. There is an implication that thoughts, feelings and behaviours could be a perpetuating or causal factor in ME, which is not proven. Furthermore, due to the paucity of evidence of clinical benefit from CBT, for which the central tenet is behavioural change, this could actually be considered disproven. We strongly request you remove this part, the next bullet point covers what is said here far more appropriately.	Thank you for your comment. The committee agreed that this bullet point was important to include and this was the basis of a holistic approach to the care of people with ME/CFS.
ME Action UK	Guideline	034	019	We agree with this bullet point, and are pleased to see it's inclusion.	Thank you for your comment.
ME Action UK	Guideline	034	023	Under positive experiences of CBT identified in the qualitative evidence it is found that: "people were comforted by the knowledge that the therapist was available if they needed help as a form of safeguard." (Evidence Review G p325 line 6) By defining CBT as a time-limited intervention this removes one of the few positive experiences identified. Again, it appears that	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any

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				generalised psychological support is more appropriate than this intervention, as it more broadly covers the wants and needs of people with ME and can provide an ongoing relationship with a therapist.	recommendations for any of the interventions (see evidence reports G and H). CBT is a time-limited intervention and the positive experiences were reported in the context of receiving CBT. Describing CBT as time-limited does not remove the interpretation of these positive experiences.
ME Action UK	Guideline	034	028	We agree with this bullet point.	Thank you for your comment.
ME Action UK	Guideline	035	General	We remain concerned that unless there is a significant effort to retrain existing healthcare professionals delivering services, the recommendations here will make little difference to the service provided. We acknowledge that energy management in people with ME could theoretically be supported via CBT but it is unlikely that people previously trained to use CBT to treat ME would simply switch to this approach, and considering the "lack of clarity over the intervention components" this acknowledgement remains entirely theoretical. We request that when considering these recommendations prior to publication of the final Guideline, the committee takes account of the level of shift required to achieve high quality care and support for people with ME.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
ME Action UK	Guideline	035	025 - 026	Again, we strongly advise against the use of the term 'goals'. Evidence Review G (p336 line 26) states: "The committee noted that where goals are rigid and unrealistic this can result in false starts, flares and relapses. The committee commented on the findings in the qualitative evidence that people had felt pressured and blamed when they could not complete the programme even though it was making their symptoms worse. The committee	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how

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				acknowledged the controversy around the setting of fixed unrealistic goals and the importance of understanding realistic goal setting by both the person with ME/CFS and the healthcare professional supporting any programme." Whilst this was in relation to physical activity, the term remains problematic across the board. We are particularly surprised that the committee have not even included the term 'realistic goals' here. This sentence would be more appropriate if it removed mention of goals leaving: "Healthcare professionals delivering CBT to a person with severe or very severe ME/CFS should adjust the process and pace of CBT to meet the person's needs. This might include shorter and less frequent sessions."	CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations.
ME Action UK	Guideline	035	001	We agree with this bullet point.	Thank you for your comment.
ME Action UK	Guideline	035	003	We cannot find an evidence base to support this bullet point. The phrase "exploring their personal meaning of symptoms and illness" is unclear. None of the positive aspects of CBT identified appear to relate to "personal meaning of symptoms". Furthermore we are concerned that inclusion of this could lead to therapists imposing their own stigmatised views and meanings onto the person with ME - as Evidence Review G (p325 lines 33-38) notes that experiences of CBT included perceptions of CBT as 'controlling, patronising and a form of brainwashing'. Remove this bullet point.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS, •exploring the personal meaning of their symptoms and illness, and how this might relate to how they manage their symptoms is an important component of CBT and the committee agreed that it should remain in the recommendation. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations.

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ME Action UK	Guideline	035	008	This bullet point creates significant confusion, as this Guideline has already advised a management plan be devised in collaboration with a specialist team. We therefore recommend changing this bullet point to: "working together to adjust and refine strategies to adapt to living with a long-term illness"	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
ME Action UK	Guideline	035	009	In recommendation 1.11.46 this Guideline states that CBT is a "time-limited intervention". However, this recommendation states that CBT should include "reviewing their plan regularly to see if their self-management strategies need to be adapted, for example if their symptoms or functioning change" In Evidence Review G one of the themes relating to a positive experience of CBT was ongoing support - "people were comforted by the knowledge that the therapist was available if they needed help." (p325 line 6) This factor is important, and is common across other modalities of psychological support. It should not be explicitly excluded by the use of a time-limited therapy simply because more research has been done on CBT, not because it is shown to be more effective. Again, focusing only on CBT in this section would mean the omission of this important point for professionals considering support for people with ME. As the term "management plan" has already been used under recommendation 1.5.2 and is separately defined in this Guideline, we strongly urge the committee to focus in this section instead on the development of strategies. It is the case that a plan is generally fixed until the situation changes whereas good strategies for adapting to symptoms will always be good	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan. CBT is time-limited but within this period includes review and adaptions where appropriate. CBT is a time-limited intervention and the positive experiences were reported in the context of receiving CBT. Describing CBT as time-limited does not remove the interpretation of these positive experiences.

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				strategies. Reviewing and changing a plan only after symptoms or functioning have changed could cause additional harm if the person's energy envelope has reduced. Change this sentence to: "reviewing their strategies regularly to see if they need to be adapted, and ensure the strategies are appropriate if they experience a change in symptoms or functioning"	
ME Action UK	Guideline	035	012	"Therapy blueprint" appears to be an obscure term that most non-experts will not understand. As this Guideline is intended for people with ME, general health professionals and the public, we see its use as unhelpful. We therefore request the use of plain English here instead.	Thank you for your comment. A therapy blueprint is specific to CBT, it is collaboratively developed between therapist and patient at the end of the course of therapy. The purpose of the blueprint is to summarise the course of therapy and strategies used, to provide a basis for future independent self-management and facilitate continued progress. A definition has been included in the guideline.
ME Action UK	Guideline	035	015	We note again that there is not a clear statement on the risks here, meaning that health professionals without in-depth knowledge will not be able to give their patients the information they need in order to give informed consent. We were particularly alarmed to find in Evidence Review G that "[t]asks were often initially very hard to achieve, and parents found it challenging to watch their children push themselves." (p325 line 20) This directly contravenes the advice on energy management this committee has agreed is key. A statement similar to that made for physical activity should be included here too; e.g. "Explain that some people with ME/CFS have found that cognitive behavioural therapy can make their symptoms worsen, for some people it makes no difference and others find it helpful."	Thank you for your comment. The committee agree it is important for the risks and benefits to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that you highlight and be able to support the child or young person and their parents or carers to make an informed choice. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS

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					is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
ME Action UK	Guideline	035	019	We strongly agree that parents and carers should be involved wherever possible, and urge the committee to retain this sentence.	Thank you for your comment.
ME Action UK	Guideline	035	022	Given that the severity of the cohorts assessed was usually unclear, the evidence base for the use of CBT in severe or very severe ME is in even muddier waters. Many of the studies required attendance at a clinic, which excludes most people with severe or very severe ME from inclusion. Moreover, the effort and energy involved in getting out of the house and to a clinic increases the risk of an adverse response to the intervention. We therefore request that a caveat be inserted here that acknowledges CBT can be unsuitable and harmful for people with severe and very severe ME. Evidence Review C (p73 line 36) shows that hypersensitivity to noise can make CBT impossible for many severe sufferers: "The committee discussed the importance of energy management for people with ME/CFS and the prioritisation of daily activities. They commented that this is heightened in people with severe and very severe ME/CFS where even the smallest action or interaction may result in worsening of symptoms. People with severe or very severe ME/CFS report they can be hypersensitive to noise and even people whispering can be very painful."	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or focusing for periods of time can be difficult, and particularly so for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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				Add a recommendation such as: "Be aware that if cognitive behavioural therapy is outside the person with ME's energy envelope it is contraindicated."	reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person. *Risks* The committee agree it is important for the risks and benefits to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that you highlight and be able to support a person with severe or very severe ME/CFS make an informed choice.
ME Action UK	Guideline	036	002	While we agree with what is included here, consideration must also be given to energy management, especially where existing treatment modalities are contraindicated in ME - such as taking regular physical exercise for depression. We ask that you add the part in bold to this recommendation: "Take into account the recommendations in the section on principles of care for people with ME/CFS, the section on access to care and the section on energy management when managing coexisting conditions in people with ME/CFS."	Thank you for your comment. Energy management has been added to the recommendation advising that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and should be taken into account.
ME Action UK	Guideline	036	007	We welcome the signposting to guidance on multimorbidity, thyroid disease and coeliac disease.	Thank you for your comment. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not

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				However, in the feedback we have received as we have written this response, people with ME have requested the addition of further conditions here. A study of comorbidity in ME/CFS concluded that "[o]ver 80% of a large population-based cohort of Spanish patients with ME/CFS presented comorbidities" and that "a thorough assessment of comorbidities is mandatory in view of their specific involvement in the deterioration of the quality of life of these patients."[1] Another study found that 97% of ME/CFS subjects had been diagnosed with at least one of 43 listed medical conditions.[2] This must be emphasised in order to ensure that symptoms are not wrongly assumed to relate to ME. As Evidence Review C states, "Patients often felt they needed to take a proactive role in their care by doing their own research to persuade health- professionals to meet their needs, by asking for diagnostic tests, seeking treatment elsewhere, turning to private or alternative health services, and in some cases withdrawing from services and managing symptoms themselves." This is reflected in Evidence Review D (p65 line 37): "The committee agreed the importance of performing relevant tests for differential diagnoses, both pre- and post-diagnosis of ME/CFS. It was considered that new symptoms can develop after a diagnosis and that these should still be fully investigated rather than immediately attributed to ME/CFS. During investigation of new symptoms, both differential and comorbid diagnoses should be considered where appropriate." (Our emphasis.) Overall, the input we've received suggests that GPs rarely have the time or experience to thoroughly investigate and manage coexisting conditions, and that without a more extensive list of these, accurate identification of differential and coexisting conditions will remain limited.	infer any importance of the condition in reference to co-existing with ME/CFS. After considering the stakeholder comments the committee removed the reference to the NICE guideline on Coeliac disease and added the NICE guideline on irritable bowel syndrome in adults. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline.

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				Serious consideration should be given to diagnosing and treating common comorbid conditions, such as those laid out in the International Consensus Criteria[3] or Canadian Consensus Criteria[4]. 1. Castro-Marrero, J., Faro, M., Aliste, L., Sáez-Francàs, N., Calvo, N., Martínez-Martínez, A., ... & Alegre, J. (2017). Comorbidity in chronic fatigue syndrome/myalgic encephalomyelitis: a nationwide population-based cohort study. Psychosomatics, 58(5), 533-543. 2. Chu, L., Valencia, I. J., Garvert, D. W., & Montoya, J. G. (2019). Onset patterns and course of myalgic encephalomyelitis/chronic fatigue syndrome. Frontiers in pediatrics, 7, 12. 3. Carruthers, B. M., van de Sande, M. I., De Meirleir, K. L., Klimas, N. G., Broderick, G., Mitchell, T., ... & Bateman, L. (2011). Myalgic encephalomyelitis: international consensus criteria. Journal of internal medicine, 270(4), 327-338. Carruthers, B. M., Jain, A. K., De Meirleir, K. L., Peterson, D. L., Klimas, N. G., Lerner, A. M., ... & Sherkey, J. A. (2003). Myalgic encephalomyelitis/chronic fatigue syndrome: clinical working case definition, diagnostic and treatment protocols. Journal of chronic fatigue syndrome, 11(1), 7-115.	
ME Action UK	Guideline	036	012	To make it clear that depression, anxiety or other mood disorders are responses to living with a debilitating disease we recommend changing the word "associated" to "reactive" here.	Thank you for your comment. 'Associated' reflects that depression, anxiety or other mood disorders can be present in people with ME/CFS and is appropriate here and for this reason this has not been edited.
ME Action UK	Guideline	036	014	As this ME Guideline is literally about a chronic physical illness, the inclusion here of the Guideline on depression for those without a chronic physical health problem is superfluous.	Thank you for your comment. This section links to the NICE guidance on co-existing conditions and it is important that people with ME/CFS that also have associated conditions receive appropriate treatment for them.

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				Furthermore, inclusion of this Guideline is problematic because standard questionnaires used for assessment of depression currently include questions relating to having little energy, trouble concentrating and trouble sleeping and can give rise to a mistaken diagnosis of depression in people with ME. We request you remove this bullet point. NICE must recommend that while it is possible for people with ME to be depressed, doctors must take note of whether reported symptoms associated with depression are in fact symptoms of ME itself. Comparison of SF-36 physical function, social role function, and emotional role function to more simplistic depression questionnaires may be salutary.	Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. For this reason this bullet point has not been removed.
ME Action UK	Guideline	037	003	During discussion online and during the community calls #MEAction UK ran to discuss this draft Guideline, some felt the term "flare" was acceptable while others did not. There was a general feeling that "crash" was the terminology most used by people with ME, and this should at least be mentioned alongside the term "flare". This is especially true as people also use this term when speaking with healthcare professionals, and they therefore need to be aware of this. Some questioned why an additional term of flare was being used as well as PESE, and felt it would be simpler to replace flare with PESE throughout. We also note that in the input we have received, multiple people have said their experience of PEM/PESE or flares is longer than a few days. In the definition of this term, we note the committee states "it may not be clear in the early stages of a symptom exacerbation whether it is a flare or a relapse." (Guideline p44 line 26)	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. The definition in the terms used in the guideline on flare up includes reference to PEM recognising that flare ups usually occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note the definitions clarify the difference between a flare up and relapse and for this reason your suggestion has not been added to the recommendation.

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				If this recommendation around flares is retained, it must therefore include an additional sentence stating: "Be aware that it may not be clear in the early stages of symptom exacerbation whether it is a flare or relapse." This will ensure the potential long term impacts of relapse are considered at the earliest possible time point.	
ME Action UK	Guideline	037	012	We suggest the use of the term 'resuming' in place of 'increasing'.	Thank you for your comment. This has been edited to, 'returning'.
ME Action UK	Guideline	038	001	We are concerned here that this recommendation comes too late for many people. Once in a relapse, accessing services and support will be significantly harder for the person with ME. Having strategies in advance of a relapse is key here. We recommend adding an additional recommendation stating: "Give all people with ME information on strategies to use in a relapse, and discuss how they may utilise these, such as: ● reducing, or stopping, some activities ● increasing the frequency or duration of rest periods ● re-establishing a reduced energy envelope to stabilise symptoms" During a relapse, offer to discuss these strategies."	Thank you for your comment. This recommendation has been edited and makes it clearer that the strategies are discussed with the person and included in the care and support plan to help them respond promptly if they have a flare up or relapse.
ME Action UK	Guideline	038	005	The Guideline recommends "re-establishing a new energy envelope to stabilise symptoms." The use of the term "energy envelope" here is incorrect - as per the definition on page 42, the energy envelope is "the amount of energy a person has to do all activities without triggering an increase in their symptoms." This is not something that can be established by the person with ME; instead we suggest using language from the section on energy management that discusses activity patterns. It is also important to emphasise here that the energy envelope will have	Thank you for your comment This has been edited to, 'reassessing energy limits to stabilise symptoms.' with the focus of the recommendation on reducing activity and resting. The committee hopes this adds further clarity. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of

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				reduced, and a concurrent reduction in activity is required to guard against further relapses. This should state: "re-establishing a reduced activity pattern to stabilise symptoms."	energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
ME Action UK	Guideline	038	012	This section deals with treatment after a relapse but seems to assume that it is safe for people taking part in a physical activity programme to resume, even at a lower level. This is dangerous advice for someone with ME. The aim of any programme should be to stabilise and to reduce relapses that often cause a decline in function. If a physical activity programme causes relapses or flares then it has no place in a Guideline on ME. There remains an underlying assumption in this Guideline that 'increases' or 'goals' have a part in the management of ME. However, the core principle of care and management should be 'stabilisation'. This will reduce or avoid worsening of symptoms.	Thank you for your comment. The reference links to the section on physical activity section and includes reference to the importance of this being overseen by a physiotherapist with training and expertise in ME/CFS.
ME Action UK	Guideline	039	001	Have the committee given consideration to recommending GP practices keep a register of people diagnosed with ME, and especially those with severe or very severe ME, in order to aid review and care of this population in line with the other recommendations made here?	Thank you for your comment. The development of a registry was not identified as a priority area in the scoping phase of the guideline and not included in the scope. As such the committee did not review the evidence and were unable to make a recommendation for a GP register.
ME Action UK	Guideline	039	002	We strongly agree with the recommendation of a yearly review and would like to see home visits or online appointments offered to moderate as well as severe patients as the effort involved in attending appointments can cause PEM/PESE and lead to a relapse.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments. In the Access to care section of the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME Action UK	Guideline	039	015	It is important to include here that new symptoms should always be investigated as a possible comorbidity and not just assumed	Thank you for your comment.

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				to be part of ME. Symptom labels for ME can be broad and may overlap with other energy limiting chronic conditions.	The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This has been reinforced in the flare up and relapse section of the guideline.
ME Action UK	Guideline	039	023	It should be specified that advice should be sought from an appropriate 'clinical' specialist.	Thank you for your comment. Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. As such adding clinical would not provide any further clarification and has not been added.
ME Action UK	Guideline	039	027	We welcome the recommendation in 1.14.6 that children should receive six monthly reviews and would like to see home visits or online appointments offered to moderate, as well as severe, patients, because the effort involved in attending appointments can cause PEM/PESE and lead to a relapse - as outlined in Evidence Review G p256 line 16: "There were reports that travel to the hospital site for appointments contributed to setbacks, which worsened fatigue in some young people."	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
ME Action UK	Guideline	040	011 - general	We strongly agree with the inclusion of a section on training in this guideline, and commend the committee for taking this step.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering

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				As both the evidence reviews and expert testimony identify, training for healthcare professionals on ME is often superficial or non-existent. During #MEAction UK's community call to discuss this Guideline, training of healthcare professionals was identified as one of the key aspects of this Guideline that could lead to improved care for people with ME - but only if this training is compulsory, includes retraining for professionals who are already working in this area and is adopted wholesale rather than piecemeal. Participants agreed that each GP practice should have at least one member with more extensive training on ME, as well as all specialist team members undertaking such training. Any change in approach to managing ME hinges on both the content of new training and the ability of those undertaking it to accept and alter their views accordingly. Healthcare professionals need to recognise and agree that "ME/CFS is a serious, chronic, complex systemic disease that often can profoundly affect the lives of patients and [...] is not, as many clinicians believe, a psychological problem."[1] This is confirmed by Evidence Review C p68 line C which shows that there is a lack of medical legitimacy with limited health professional knowledge and understanding of ME/CFS underpinned by insufficient medical training. Evidence Review A p42 line 8 states explicitly "disbelief of the legitimacy of the condition" is a consistent theme in all of the qualitative reviews conducted for this Guideline. In her expert testimony, Dr Nina Muirhead states "The incongruity between current education of professionals and the experience of patients compromises the relationship between patients and health and social care professionals. Or worse has the potential to cause harm" (Appendix 3 p18).	care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. It is beyond the remit of NICE to recommend compulsory training but these recommendations are a clear indication of the need for training.See evidence review B for the committee discussion on training.

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[1] Ganiats, T. G. (2015). Redefining the chronic fatigue syndrome. https://www.acpjournals.org/doi/10.7326/m15-0647

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				Current training modules need to be withdrawn immediately and replaced by new ones that are in accordance with this Guideline. Evidence Review B p51 line 23 notes that Dr Muirhead's testimony supports the weaknesses in the current training of medical staff. "Her experience has been that the information, education and support provided by medical bodies is mostly outdated, misleading and not in line with patient experience. In particular, she expressed concerns that ME/CFS training and education is not mandatory, is often merged with other medically unexplained symptoms and is based on theories of deconditioning and fear avoidance of exercise." Such a wholesale change needs action at a high level within the NHS, CCGs and health boards. It is essential that NICE urgently communicates the new recommendations on training to all current specialist clinics, all medical colleges and professional organisations of all health and social care professionals, to prevent further harm. This needs to be expedited as soon as possible alongside the production of the new Guideline. Overall we believe this section should be strengthened and expanded to emphasise the need for training/retraining of all staff, stress that the training should be based on these Guidelines and recommend that previous training should be withdrawn immediately as it has the potential to cause harm to patients.	
ME Action UK	Guideline	040	012 - 013	The phrase "access to training" suggests that training is optional, and we suggest it should be replaced by "mandatory" or "compulsory". We strongly agree that training should reflect current knowledge: for this Guideline to effect change for people with ME the development of completely new training is essential.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline.

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				We suggest that the recommendation is reworded to state "Health and care providers should provide compulsory training that reflects current knowledge in ME/CFS (including understanding what ME/CFS is, diagnosis and management) for all health and social care staff who deliver care to people with ME/CFS". We suggest a sentence is added to this recommendation stating that health providers should immediately withdraw current training based on the old Guideline in order to avoid harm to patients (Appendix 3 p18).	To note the training recommendations have been edited. See evidence review B for the committee discussion on training. It is beyond the remit of NICE to recommend compulsory training but these recommendations and discussion are a clear indication of the need for training and appropriate training materials.
ME Action UK	Guideline	040	017	We agree that training programmes must provide evidence-based content and training methods. It is great that NICE has embraced the fundamental importance of patient involvement in the understanding of this disease and development of new training programmes, however we urge the committee to include specific mention of input from ME organisations as well as from individual people with ME. Change this to: "provide evidence-based content and training methods (developed and supported by specialist services with input from people with ME and patient organisations)"	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion on training where they emphasise the importance of having .training programmes with evidence-based content and training methods.
ME Action UK	Guideline	040	018	We welcome the recommendation that training should be developed with input from people with ME, however we urge that this recommendation includes the involvement of ME organisations and charities. It is imperative that any new training programme is co-produced by professionals who have already adapted their approach to ME, based on a biomedical understanding, and ME organisations, such as the CMRC Medical Education group. Without this involvement there is a high risk of inadequate and	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion on training where the committee include discussion on how training programmes are developed. The wording ,'with input from people

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				misleading information being produced once more. This would not only be a waste of money and resources but fail to improve the care of people with ME/CFS.	with ME/CFS' this does not exclude ME and patient organisations. The development of training by ME/CFS specialist services reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS.
ME Action UK	Guideline	040	019	As noted in the Context section p72 line 7 of these Guidelines, there remains a "lack of belief and acknowledgement from health and social care professionals" both within many "specialist" clinics and more widely. Considering the major changes in practice and understanding this Guideline sets out, we believe patient organisations are best placed to lead on new training and should again be noted here. We recommend changing this to: "are run by trainers with relevant skills, knowledge and experience, and led by or involving patients and patient organisations"	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion on training where the committee include discussion on how training programmes are developed. The wording ,'with input from people with ME/CFS' this does not exclude ME and patient organisations. The development of training by ME/CFS specialist services reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS.
ME Action UK	Guideline	040	020	We agree with this recommendation.	Thank you for your comment.
ME Action UK	Guideline	040	022	We agree with this recommendation, but feel that where possible, training should also involve speaking with people with ME in person.	Thank you for your comment. The recommendation includes' other resources' and does not exclude people with ME/CFS in person.

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				We request this is changed to: "represent the experiences of people with ME/CFS, either in person or using video and other resources."	
ME Action UK	Guideline	041	001	We recommend that the word 'All' be added here so it reads 'All health and social care professionals'. This reflects Evidence review B page 51 line 47 which states that the committee made a recommendation suggesting access to training should be provided for all staff that have contact with or deliver care for people with ME. We welcome the recommendation that health and social care professionals undertake training. It is vital that this training is based on the new Guideline and that patient organisations are involved in preparing training materials.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion on training. This emphasises the need for up-to-date training programmes.
ME Action UK	Guideline	041	001	The reference to training of health and social care professionals who provide care for people with ME needs to be expanded to address the specific need for the training of professionals heading up paediatric services. We urge that NICE recommends that training programmes clearly illustrate the debilitating effects this disease has on children and young people. Anyone involved with the care of this vulnerable group must understand and accept the diverse symptoms of this disease and the limitations it imposes on daily life. They need to realise that a snapshot view, either in a clinic or online, does not reflect the daily reality and limitations of ME.They need to listen and believe young people and their parents.	Thank you for your comment. It is clear in this section that the training recommendations apply to all health and social care staff that deliver care to people with ME/CFS and a list of professionals is not necessary. People with ME/CFS includes children and young people.
ME Action UK	Guideline	041	009	We agree with this definition of activity, and consider it important to retain in the final Guideline.	Thank you for your comment.
ME Action UK	Guideline	041	012	We agree with this definition of advocate.	Thank you for your comment.
ME Action UK	Guideline	041	018	We find this definition to be very problematic. By defining carers as "unpaid" this explicitly excludes carers or PAs who may be provided by social services, and makes an incorrect assumption	Thank you for your comment. There is not an assumption that all people with ME/CFS will have family, partners or friends , it is that there is a distinction

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				that all people with ME/CFS will have family, partners or friends who are able to take on this role. Many people with ME will need adult social care to enable them to live independently, and these people should not be excluded from the recommendations around carers being allowed to join the person with ME during appointments etc. This is especially important for people with significantly reduced cognitive capacity, where excluding paid carers from information and support needs, access to appointments, etc., could lead to serious adverse impacts on care. We very strongly urge the committee to change this definition to: "In this Guideline, a carer refers to someone who provides care and support to a family member, partner, friend or client with ME."	between paid and unpaid carers and the regulations that apply to paid carers. To clarify, 'This is distinct from care workers who are paid to provide support' has been added to the definition. Neither does this exclude paid carers from information and support needs or accompanying people with ME/CFS to appointments. Paid carers, such as care workers will be included in the recommendations for health and social care professionals.
ME Action UK	Guideline	042	001	We agree with this definition.	Thank you for your comment.
ME Action UK	Guideline	042	004	We agree with this definition.	Thank you for your comment.
ME Action UK	Guideline	042	007	We agree with this definition.	Thank you for your comment.
ME Action UK	Guideline	042	010	We agree with this definition.	Thank you for your comment.
ME Action UK	Guideline	042	014	We agree with this definition.	Thank you for your comment.
ME Action UK	Guideline	042	025	During discussion online and during the community calls to discuss this Guideline, some felt the term "flare" was acceptable while others did not. There was a general feeling that "crash" was the terminology most used by people with ME, and we suggest that this should at least be mentioned in this definition. Some questioned why an additional term of flare was being used as well as PESE, and felt it would be simpler to replace flare with PESE throughout.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. In addition, 'flare ups usually occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM.' has been added for clarity to the definition of flare up. The reference to 1-3 days has been removed and 'after a few days' included.' A relapse lasts longer than a flare up' has been added to this definition.

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				We cannot find evidence that supports the involvement of a timescale in this definition. In the input we have received, multiple people have said their experience of PESE or flares is longer than 1-3 days. We recommend removing this timescale. It would be helpful to cross reference to the term "relapse" here, stating: "It may not be clear in the early stages of a symptom exacerbation whether it is a flare or a relapse; a relapse is defined below."	
ME Action UK	Guideline	043	003	In feedback that we have received as we write this submission, some felt that "management plan" overstated what is possible, and that "support plan" (as used in the NICE MS Guideline) would be more appropriate. In case the committee considers changing this term to "care plan": this does not appear appropriate as this terminology is already in use by social services.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
ME Action UK	Guideline	043	004	This definition of a management plan appears quite different from that laid out in recommendation 1.5.2 We strongly urge the committee to change this to: "The personalised management plan is developed by the specialist team after the confirmation of a diagnosis of ME/CFS and a holistic assessment. Based on the person's needs, it includes: information and support needs; support for activities of daily living; aids and adaptations; education, training or employment needs; self-management strategies; physical maintenance; symptom management; guidance on flares and relapses; and contact details for a named health and social care professional. It is the basis for all other assessments and plans."	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The definition is a summary and includes an overview of what is within the care and support plan, it is not meant to be exhaustive. For this reason you suggestions have not been added.
ME Action UK	Guideline	043	009	There has long been debate about the terminology used to differentiate between different severity levels of ME. Many feel that the term "mild", when considered against other chronic illnesses such as asthma, underplays the severity of ME.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the

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				Some felt a change of term would be appropriate here, however there was no clear consensus on what that should be. Suggestions ranged from changing to a grade/level 1-4 type terminology, or to scrapping mild and renaming this moderate, renaming moderate to severe, severe to very severe, and very severe to extremely severe. Others, including some who are would fit into this definition, felt okay with the term mild. #MEAction UK therefore cannot make a clear recommendation on changing the term from mild to something else or not. However as we cannot find a rationale for why this has been used, we felt it important to raise this point and ask the committee to consider, alongside other feedback, if this is indeed the most appropriate term.	definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
ME Action UK	Guideline	043	010	We request that the committee adds a note that "Mild ME/CFS has a significant impact on quality of life."	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
ME Action UK	Guideline	043	015	We agree with the first sentence in this definition. We also agree with the statement: "They have usually stopped work, school or college and need rest periods, …" However we cannot find an evidence base to support the assertion relating that to rest periods: "often resting in the	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more

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				afternoon for 1 or 2 hours." We feel this is an unhelpfully limiting part of the definition, that doesn't represent the broad experience of when and how much rest a person may need. We would remove this specific part of the definition. By including the statement on sleep being poor quality and disturbed in the definition of moderate but not mild or severe ME, it implies a difference in symptom presentations. Furthermore this is not accurate for every person with moderate ME - some may sleep fine, but wake unrefreshed. It would be better to focus on functioning in the definitions of mild and moderate ME. We recommend removal of the sentence on sleep. We recommend adding a sentence to state that people with moderate ME usually have difficulty leaving the house and some are mostly housebound.	severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
ME Action UK	Guideline	043	020	As this definition differs significantly from that used elsewhere, we are curious as to why the committee has focused on inability to regulate blood pressure and cerebral flow. While these can be causal factors in orthostatic intolerance, the definition of orthostatic intolerance itself normally focuses on increased symptoms, or new symptoms, on standing or sitting upright. We therefore feel it would be helpful to add an initial sentence stating this broader definition of the impact of orthostatic intolerance, before what is already defined here. "Orthostatic intolerance is an increase in symptoms or the development of new symptoms on standing, or in some cases sitting, upright. This can be caused by the inability to regulate blood pressure and cerebral blood flow when upright. It may lead to postural tachycardia, hypotension and alterations in consciousness (such as fainting). This may include postural	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as lightheadedness, near-fainting or fainting, impaired concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).

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				orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing)."	
ME Action UK	Guideline	043	027	We agree with this definition of physical activity, and particularly the sentence: "For many people, physical activity has a health benefit but in people with ME physical activity may make their symptoms worsen." We strongly urge the committee to retain this important fact in the final version. It would be helpful to note the extremely low levels of physical activity that can lead to PEM/PESE in some people with ME. We recommend the inclusion of a final sentence that states "For some people with ME physical activities such as brushing their teeth, speaking briefly, or turning over in bed will be their main physical activities of the day."	Thank you for your comment. The definition does include that physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen. The committee noted that the impact would vary in individuals with ME/CFS and agreed to leave the definition broad.
ME Action UK	Guideline	044	006	This is an excellent definition. We are particularly pleased to see the last sentence "Such activity is undertaken within the person's energy envelope and avoids pushing through boundaries of tolerance." We have made a separate comment on the physical maintenance section that this explicit statement should also be included there, to ensure those who do not read through the definitions of terms understand this.	Thank you for your comment.
ME Action UK	Guideline	044	018	There are mixed views about introducing the new term PESE into use, and because of this we do not feel we can make a clear recommendation as an organisation. Participants on our community call discussed this section of the draft Guideline, and generally agreed the term post-exertional symptom exacerbation was better than post-exertional malaise, however this was not unanimous.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of

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				Overall we agree with the committee's assessment that the word malaise underplays the severity and impact of this symptom in people with ME. Our colleagues in the US expressed concern that adding a new term would create yet another long acronym: PEM/PESE. They noted that they are getting traction with US institutions using the terminology PEM at the moment, and felt a change may lead to greater confusion. To assess general support of this change in terminology we published a poll on our social media platforms which, out of 406 respondents indicated support for the term PEM from 49%, with PESE gaining 44% and other terms 8%.	Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
ME Action UK	Guideline	044	019	We agree with the first sentence of this definition, and the note that this is also referred to as post-exertional malaise. During our community calls some attendees raised the point that in their experience PESE/PEM was not always delayed, and preferred the wording "symptoms can worsen 12 - 48 hours…" over "symptoms typically worsen 12 - 48 hours..." Others noted that they experienced some symptoms only during PEM/PESE, and therefore felt that language such as "and development of different symptoms" should be added into this statement.	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.
ME Action UK	Guideline	044	023	We agree with this definition overall. It is important to note that relapses can lead to long-term reduction in the person's functioning. We are unsure about the sentence "The person's symptoms and level of disability may be similar to illness onset." We cannot find an evidence base to support this, nor do we recognise this in our lived experience. For some, symptoms at	Thank you for your comment. The person's symptoms and level of disability may be like illness onset." has been deleted.

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				onset are severe, however for others symptoms gradually get worse. We recommend removing this sentence.	
ME Action UK	Guideline	045	021 - general	We welcome the section of Recommendations for research, but are disappointed by how sparse these recommendations are. As this committee has found, biomedical research into ME is fragmented and small-scale because of lack of funding. Although a lot of useful research has been done, there is a need for well-funded, targeted research which in many areas will involve large-scale, carefully designed and controlled trials. Making funding available for these should be a key recommendation. Investment in research would be a sound economic investment. WIth 250,000 estimated sufferers in the UK, 75% of whom cannot work, effective management or treatment tools would save healthcare costs and boost tax returns. NICE needs to send a clear message that ambitious biomedical research is needed now. In particular, this committee must make a recommendation for research into the causes of ME. While NICE may usually focus on treatment and management of illness, in this case research into treatments has stalled in part because the "pathophysiology is unclear." (Guideline p4 line 6) It is only with a clearer understanding of the pathophysiology that treatments and eventually a cure will be found. We strongly urge the committee to add a recommendation such as: "What are the causal mechanisms of ME that may lead to effective treatments?"	Thank you for your comment. Research recommendations can only be made for where the evidence has been searched for within the guideline. Biomedical research was not included in the scope of this guideline as a topic to consider, and therefore we are unable to make research recommendations on this topic.
ME Action UK	Guideline	045	001	Overall we support this definition, particularly the inclusion of two levels of severity here; severe and very severe.	Thank you for your comment.

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				While of course there is so much more that could be said about severe and very severe ME, this gives a simple but clear overview of how debilitating they are.	
ME Action UK	Guideline	045	011	Therapy blueprint is an obscure term that should not be used in this Guideline. Again there is a focus on goals for the future, despite a clear statement that CBT, under which this term is mentioned, is not a treatment or cure for ME. The committee found evidence that goal setting has been harmful for people with ME, yet do not present evidence to show that the language they are proposing to use will mitigate this, nor have they even used the language of "realistic goals" which they specify elsewhere. In the face of evidence of harm, there must be very clear evidence that benefit outweighs the harm of such approaches. We cannot see that the committee has done their due diligence in this respect. It is not clear what "warning signs" mean here, nor why it is in quotation marks. We encourage the committee to remove this term from the whole Guideline.	Thank you for your comment. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose of explaining these would be included in the blueprint. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.
ME Action UK	Guideline	045	017	We cannot find any evidence that describes unrefreshing sleep as a light sleep. Nor can we find significant evidence to suggest that 'light sleep' truly describes the experience of unrefreshing sleep for most people with ME. In Box 1 in the section on Symptoms for suspecting ME/CFS, it is instead described as 'feeling exhausted, flu-like and stiff on waking' and as 'broken or shallow sleep, altered sleep pattern or hypersomnia'. We therefore suggest the removal of this first sentence and believe it is instead best to stick to the facts in the second two sentences.	Thank you for your comment. After considering the stakeholder comments, this definition has been edited to,' Unrefreshing sleep means that is non-restorative. Even after a full night's sleep people do not feel refreshed. People with ME/CFS often report waking up exhausted and feeling as if they have not slept at all, no matter how long they were asleep.' to aid further clarity.
ME Action UK	Guideline	045	024	We strongly welcome the two key recommendations for research into diagnostic tests and a core outcome set. The core outcome set in particular is vital to be able to standardise research findings, to ensure objective measures are	Thank you for your comment.

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				used as well as any subjective measures, and to ensure findings of minimal clinical difference genuinely reflect what people with ME consider important changes in their health and wellbeing.	
ME Action UK	Guideline	046	004	The other research recommendations for diagnostic criteria and dietary strategies are helpful, but otherwise these recommendations relate to "management" and "non-pharmacological" interventions. There is a lack of research recommendations relating rigorous biological science, looking for causes, mechanisms and treatments, many of which will likely be pharmacological. In particular participants in our consultation process have commented on the need to move towards objective measures and away from subjective measures as the primary outcome of ME studies. One participant said "By the next review we need much better quality research as evidence, not another decade of wasting the limited money available."	Thank you for your comment. The research recommendations are developed from the evidence reviews and as evidence looking for causes and mechanisms of ME/CFS was not reviewed the committee were unable to make a research recommendation on this topic. The committee agree there needs to be a core outcome of relevant health outcomes and have made a research recommendation for this topic.
ME Action UK	Guideline	046	004	Add recommendation: What is the clinical and cost effectiveness of medicines and supplements in the management of symptoms in ME? While the committee found many small trials on pharmacological treatment, quality of evidence was often low, sample sizes small, and outcomes therefore dubious. Further research is needed here urgently, as this could be the first area to create significant improvements in the quality of life of people with ME.	Thank you for your comment. *Medicines* The committee recognised the lack of research in medicines but did not identify any one medicine or supplement to prioritise for research and as such did not make any research recommendations on this topic.
ME Action UK	Guideline	046	004	Add recommendation: What is the clinical and cost effectiveness of treatments for orthostatic intolerance in ME?	Thank you for your comment. The research recommendations are developed from the evidence reviews and as this evidence was not reviewed the committee were unable to make a research recommendation on this topic.
ME Action UK	Guideline	046	004	Add recommendation: What is the clinical and cost effectiveness of treatments for nausea in ME?	Thank you for your comment.

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ME Action UK	Guideline	046	004	Add recommendation: What conditions commonly coexist alongside ME?	Thank you for your comment. The research recommendations are developed from the evidence reviews and as this evidence was not reviewed the committee were unable to make a research recommendation on this topic.
ME Action UK	Guideline	046	004	Evidence Review A p6 line 23 states "No evidence was identified for social care professionals caring for people with ME/CFS." Add two recommendations: ● What information and training do social care professionals caring for people with ME require? How can social care professionals caring for people with ME best meet their needs?	Thank you for your comment. The section on training includes both health and social care professionals. The committee have not been detailed in the content of the training programmes so programmes can be reflective of professionals needs. The recommendations in the guideline apply to health and social care professionals. They should be taken into account by social care professionals when caring for people with ME/CFS. On this basis the committee did not make a research recommendation specifically aimed at social care professionals.
ME Action UK	Guideline	046	004	The Equality Impact Assessment states that "the groups identified in the equalities impact assessment during scoping were considered through the development of the guideline, however there was no or limited evidence identified for these groups and it was agreed no separate recommendations for these groups were to be made". (These groups are listed as: Older people; Pregnant women; Black and Minority Ethnic people; and Men, as well as those from low socioeconomic backgrounds and those living in rural settings. *Equality Impact Assessment questions 1 & 2*.) In light of this concerning lack of evidence, we recommend adding a research recommendation considering access to care and outcomes for people with ME in groups with potential equality issues.	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'Be sensitive to the person's socioeconomic, cultural and ethnic background, and faith group,

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					and think about how these might influence their symptoms, understanding and choice of management.' to recommendation 1.1.3. *Recommendations for research* To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
ME Action UK	Guideline	046	005	Due to the cognitive difficulties and severely limited energy people with ME experience, it would be helpful to add specific mention of automated technologies to this research recommendation. We recommend this is changed to: "What is the clinical and cost effectiveness of self-monitoring techniques, such as automated technologies, apps and wearables, in guiding energy management in ME?"	
ME Action UK	Guideline	047	002	This recommendation is quite concerning, as it seems to suggest a behavioural approach to managing ME, without recognition of the evidence found by this committee that demonstrates behavioural approaches have very poor outcomes. This recommendation doesn't even apply to managing symptoms in ME, but to managing ME as a whole. We have anecdotal reports, and experience within our team, that past use of sleep management strategies have harmed people with ME, including children and young people. We strongly recommend this recommendation is changed to "What is the clinical and cost effectiveness of medications to manage unrefreshing sleep and other features of abnormal sleep in ME?"	Thank you for your comment. A lack of evidence was identified on sleep strategies and this research recommendation reflects the need for research on this topic. Medication is included in the research recommendation (see evidence review H- non pharmacological management appendices).
ME Action UK	Guideline	071	015 - 017	We agree with the inclusion of this sentence on prevalence.	Thank you for your comment.

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ME Action UK	Guideline	071	020 - 022	We agree with the inclusion of these sentences.	Thank you for your comment.
ME Action UK	Guideline	071	009	We welcome the inclusion of the context section.	Thank you for your comment.
ME Action UK	Guideline	071	012	We dispute that there being “little pathological evidence of brain inflammation[...] makes the term 'myalgic encephalomyelitis' problematic.” In our experience, people with ME have experienced far greater problems in having a disease with multiple names, including “chronic fatigue syndrome”, a name that is trivialising and focuses on one symptom at the expense of many others. Various diseases have historical names that do not accurately describe the disease entity, malaria being one such example that is a contracted form of *mala aria* ‘bad air’. We continue to oppose using the term chronic fatigue syndrome (CFS), and considering this committee is at present recommending new terminology such as PESE, energy envelope, energy management and more, we strongly urge them to make a recommendation that this disease is called myalgic encephalomyelitis (ME). As committee members have recognised, people with ME have faced significant stigma. The term CFS has contributed to this. We strongly urge the committee to take an active stance on this issue, instead of passively accepting an outdated misnomer that they recognise here to be considered “too broad, simplistic and judgemental.”	Thank you for your comment. The committee agrees there is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *‘This guideline scope uses ‘ME/CFS’ but this is not intended to endorse a particular definition of this illness, which has been described using many different names*’ and then readdressed in the context section of the guideline, *‘The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.’*
ME Action UK	Guideline	071	019	We strongly urge the committee to replace “emotional wellbeing” with “physical functioning” here. The focus on emotional wellbeing is unfounded, with some evidence suggesting that, “[p]erhaps surprisingly, mental health was less affected in patients with CFS.”[1]	Thank you for your comment. This sentence has been edited in line with the rest of the guideline where emotional wellbeing is to ‘significant impact on a person’s quality of life, including their psychological, emotional and social wellbeing’.

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				In fact across multiple studies considered in a 2010 systematic review, "role emotional" and "mental health" sub-domain scores on the SF36 showed the smallest difference from non-ill controls.[2] Physical functioning is the factor that brings down quality of life scores so significantly, with a 70.1 point difference out of a total of 100 for the "role physical" sub-domain of the SF36.[2] This must be the focus of this sentence. 1. Maroti, D., & Bileviciute-Ljungar, I. (2018). Similarities and differences between health-related quality of life in patients with exhaustion syndrome and chronic fatigue syndrome. *Fatigue: Biomedicine, Health & Behavior*, *6*(4), 208-219. Jason, L., Brown, M., Evans, M., Anderson, V., Lerch, A., Brown, A., ... & Porter, N. (2011). Measuring substantial reductions in functioning in patients with chronic fatigue syndrome. *Disability and Rehabilitation*, *33*(7), 589-598.	
ME Action UK	Guideline	071	023	The sentence noting the lower quality of life of people with ME compared with other severe chronic conditions is an important issue in the context of ME. We would like to see this noted in the principles of care section on p4 line 8.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
ME Action UK	Guideline	071	026	This is an important paragraph to include and we are pleased to see it here. We believe it would also be helpful for clinicians suspecting ME to be aware that it can be triggered by an infection, and would like to see this stated in the section on Suspecting ME/CFS p8 line 1.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
ME Action UK	Guideline	072	003 - 006	We suggest deletion of the part of this sentence striked out. "Fatigue associated with another chronic disease may be confused with ME/CFS and some practitioners are reluctant to positively diagnose ME/CFS~~ when no other causes are found~~."	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.

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				Even in the 2007 Guideline, diagnosis was made on the presence of a defined symptom set. It was not and is not a diagnosis purely of exclusion. This sentence leads to confusion, and would be clearer noting the factual statement that practitioners are reluctant to positively diagnose ME. We hope this Guideline will go some way to changing that.	
ME Action UK	Guideline	072	007 - 009	Beyond what is written here, the lack of belief and acknowledgement from professionals may lead to worse outcomes. We recommend adding the parts in bold: "People with ME/CFS report a lack of belief and acknowledgement from health and social care professionals about their condition and related problems, which may lead to worse outcomes, and to them being dissatisfied with care and disengaging from services."	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
ME Action UK	Guideline	072	001	We agree with the inclusion of the first sentence of this paragraph.	Thank you for your comment.
ME Action UK	Guideline	072	012	We believe this paragraph should be removed. While it may have been important to the context during the scoping phase, it is no longer needed here, and sows confusion around the recommendations this committee has made. The ME community needs a clean break from a presentation of these therapies as controversial, and to be enabled to move forwards to campaign and advocate for research into treatments that will lead to a cure.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
ME Action UK	Guideline	072	019	We very much welcome the commitment from NICE to review this Guideline once further evidence has emerged from recently started studies.	Thank you for your comment.
ME Action UK	Guideline	072	022	We agree with this final paragraph.	Thank you for your comment.
ME Research UK	Guideline	General	General	ME Research UK would like to express its gratitude to the members of the guideline committee for their time and effort in producing this draft, which we consider a significant improvement on the previous guideline. In the context of an acknowledged lack of firm evidenceregarding many of the aspects covered, we feel	Thank you for your comment.

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				that the recommendations are generally pragmatic and thoughtful, showing awareness of the concerns of people with ME/CFS. We particularly applaud the removal of graded exercise therapy as a recommended management strategy.	
ME Research UK	Guideline	001	009	We are concerned that the following wording is misleading: 'This guideline will update…'. It should state that: 'This guideline will replace NICE guideline CG53 (published August 2007)'.	Thank you for your comment. This has been edited to, 'this Guideline will update and replace NICE Guideline CG53 (published August 2007)'.
ME Research UK	Guideline	004	005	We are concerned that use of the term 'medical condition' is not appropriate and should be replaced by 'disease', here and throughout the guideline. ME/CFS is a recognised neurological disease classified by WHO ICD10 G93.3. This classification is also recognised by the Department of Health and Social Care. It is also recognised as a disease by all of the US authorities and by many researchers.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease. Reference to the ICD10 classification has been included in the context section of the guideline.
ME Research UK	Guideline	004	017	Add – 'stigmatised by people (including healthcare professionals) who do not understand…'	Thank you for your comment. This has been edited to include 'family, friends, health and social care professionals and teachers'. This reflects the similar recommendation in the additional principles for the care of children and young people.
ME Research UK	Guideline	005	012	We suggest that regular monitoring and review should also be specified for people who are severely affected. Add – 'or are severely affected' to this point.	Thank you for your comment. This has been revised to, when their symptoms are worsening, changing or are severe'.
ME Research UK	Guideline	008	017	We suggest that the order of listed key symptoms be changed to: (1) post-exertional symptom exacerbation, (2) fatigability, (3) unrefreshing sleep, (4) cognitive difficulties. The undue emphasis on fatigue over muscle weakness/pain and other symptoms is a longstanding concern of many people with ME/CFS.	Thank you for your comment. The symptoms are all required for suspecting ME/CFS and are not in any order of priority.
ME Research UK	Guideline	009	002	We suggest adding 'vision-related symptoms' and 'gastrointestinal problems' to the list of other symptoms associated with ME/CFS. These can be significant problems for many people with ME/CFS (e.g. Hutchinson et al, Br J Ophthalmol, 2014, 98:144–5; Eaton-Fitch et al, Qual Life Res, 2020, 29:1521–31).	Thank you for your comment. The committee discussed the other symptoms you suggested should be on the list and they agreed to add gastrointestinal symptoms to the list. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that visual related symptoms should be included in the list

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					of associated symptoms. The committee note that visual disturbances are highlighted in recommendations within the guideline with reference to the description of symptoms.
ME Research UK	Guideline	010	002	Does 'appropriate specialist' refer to an ME/CFS specialist or someone able to advise on specific symptoms? If the latter, perhaps this could be expanded as there may be some uncertainty as to which specialties are most relevant.	Thank you for your comment. Appropriate specialist here refers to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist. The committee discussed the addition of examples of specialists but came to the conclusion that any list could not be exhaustive and there is the risk that the examples given are seen as the only specialists to refer to. For this reason the committee did not add your suggestion.
ME Research UK	Guideline	013	012	We suggest that, where possible, home visits should be from a healthcare professional with experience in managing ME/CFS patients,	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
ME Research UK	Guideline	013	016	We suggest that the 'variety of formats' should include provisions – such as large print – for people with reading difficulties, which are common in people with ME/CFS.	Thank you for your comment. As with all examples in recommendations they are not meant to be exhaustive and the link to the NICE guidelines on patient experience in adult services has further information on communication.
ME Research UK	Guideline	014	016	Replace 'a fluctuating medical condition…' with 'a fluctuating disease'	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease.

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ME Research UK	Guideline	014	018	There is a significant body of evidence showing that symptoms can be exacerbated by exertion including physical activity. Add – 'and can be exacerbated by exertion including physical activity' to this point.	Thank you for your comment. This recommendation is to give an overview of ME/CFS and there is more detail throughout the guideline on aspects of ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later in the energy management section of the guideline and for this reason your suggestion has not been added to the recommendation.
ME Research UK	Guideline	014	031	We suggest adding another item to this list – 'Explain that ME/CFS does not currently have any recommended treatment or cure'	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However the committee agree there currently isn't a cure for ME/CFS and it is important that people with ME/CFS are aware of this.
ME Research UK	Guideline	023	006	We suggest expanding on who the 'specialist team' should comprise – ME/CFS specialists or specialists able to advise on specific symptoms.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the

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					management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
ME Research UK	Guideline	027	002	We suggest adding 'neurological health' to this list; neurological health covers several potential symptoms of the disease.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
ME Research UK	Guideline	028	007	We welcome the removal of graded exercise therapy (GET) as a recommended treatment for ME/CFS. There is only limited clinical-trial evidence showing small (possibly non-specific) effects in people with the disease, while in a recent patient survey (and in several previous surveys) a majority of patients reported a deterioration in physical health after GET.	Thank you for your comment.

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ME Research UK	Guideline	028	007	Add – 'for example graded exercise therapy (or similar, analogous intervention)'	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. . The committee recommended that physical activity or

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					exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
ME Research UK	Guideline	034	General	As acknowledged in the draft guideline, cognitive behavioural therapy (CBT) cannot be considered a treatment or cure for ME/CFS, and it has only proved helpful to some people with the disease. We are therefore concerned that there is an unbalanced and excessive description of CBT in this section. By way of comparison, NICE Guideline CG186 paragraph 1.5.5 states 'Consider mindfulness-based training, cognitive behavioural therapy or fatigue management for treating MS-related fatigue.' We suggest that CBT similarly only warrants the sentence on page 34 line 2 of this guideline, as an option for symptom management. The additional detail included gives CBT undue emphasis.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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					To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
ME Research UK	Guideline	040	017	Add – 'provide up-to-date, evidence-based content…'	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. This emphasises the need for up-to-date training programmes. To note the training recommendations have been edited. See evidence review B for the committee discussion on training.
ME Research UK	Guideline	046	General	We suggest that the following should also be considered as recommendations for research: (1) Research into the pathophysiological basis of ME/CFS; (2) Are there specific subgroups of people with ME/CFS with different symptom profiles or outcomes who might benefit from different management strategies or treatments? (3) Research into predictors of severity and outcome; (4) Should clinical and research diagnostic criteria be aligned, and, if so, how? (5) How do different diagnostic criteria affect the identification and treatment of ME/CFS in clinical practice? (6) What outcomes are important at different stages or severities of disease?	Thank you for your comment. Research recommendations can only be made for where the evidence has been searched for within the guideline. Biomedical research was not included in the scope of this guideline as a topic to consider, and therefore we are unable to make research recommendations on this topic. The committee have made recommendations to address the difficulties and limitations in diagnosing ME/CFS (see Evidence review D for the committee discussion on this). The committee identified these as high priority for research. This committee hope this will enable future research to accurately identify people with ME/CFS and determine the impact of interventions on them. They thought this was particularly important before

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					recommending any research trials on physical activity or exercise interventions.
National Council for Osteopathic Research	Evidence review G	342	035 - 044	The guideline committee make the following recommendation: *'do not' offer recommendations for CBT, therapy based on physical activity or exercise therapies derived from osteopathy……* We would like to object to this statement as osteopaths are, if trained, quite capable and competent at delivering components of the interventions proposed in the guidance (Taylor SJC, Carnes D, Homer K, Pincus T, et al. Improving the self-management of chronic pain: COping with persistent Pain, Effectiveness Research in Self-management (COPERS). Southampton (UK): NIHR Journals Library; 2016 Sep. PMID: 27656730).	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However, no evidence was identified to support recommending osteopathy treatments, for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
National Council for Osteopathic Research	Evidence review G	342	027 - 031	We concur with the team the following: *'Overall the evidence for non-pharmacological interventions as a treatment for ME/CFS is inconclusive with heterogenous treatment effects and uncertainty around the effect estimates being high. There is little evidence for most of the interventions identified and most of the evidence is not consistent showing some clinical benefit but also no clinical difference across outcomes and studies.'*	Thank you for your comment.
National Council for Osteopathic Research	Evidence review G	342	035	The committee quite rightly object to those making claims about cures (Page 342 line 35), however making claims about cures is relevant to all health care professionals not just a few. Making false claims about cures, comes under the jurisdiction of the Advertising Standards Authority and the GOsC as the regulator of osteopaths for 'false or misleading advertising'. The content of the intervention delivered under name 'The Lightening Approach' is an intervention delivered by a handful of osteopaths, it seems extreme to dismiss a whole profession based on the work of a few (and one qualitative study) for an intervention that actually does appear to have some of the very components the guidance is recommending (CBT). It appears that this recommendation is not based on the evidence, as Page 342 lines 27-31 states that	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.

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				the evidence around treatment and care is of low quality and is inconsistent and inconclusive. It is accurate to state there is no cure but it is not evidence based to recommend that osteopathy derived interventions (all?) are any less effective than other interventions.	*Therapies derived from osteopathy* After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. However no evidence was identified to support recommending osteopathy treatments, for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any recommendations for treatments based on osteopathy.
National Council for Osteopathic Research	General	General	General	Please state throughout the guidance that osteopathy is an allied health profession. Since 2017, osteopathy has been recognised as part of the Allied Health Professions it is no longer classed as an alternative or complementary therapy in England and Wales (https://www.england.nhs.uk/ahp/role/). Osteopathy is a statutory regulated profession, regulated by the General Osteopathic Council (osteopathy.org.uk) under the auspices of Privy Council. Patients treated by a GOsC registered osteopath are afforded the same protection as they would have if they visited a GP, dentist or physiotherapist.	Thank you for your comment. Osteopathy is described by the NHS website as an example of complementary and alternative treatments https://www.nhs.uk/conditions/complementary-and-alternative-medicine/.
National Council for Osteopathic Research	General	General	General	The terms alternative and complementary for the description of therapies is mixed and inconsistent throughout the guidance.	Thank you for your comment. This has been standardised to 'complementary and alternative therapy'.
National Council for Osteopathic Research	Guideline	013	004	We note the preference and needs of the patient are to be considered. Preserving patient choice is fundamental to this concept, therefore we suggest that this choice should include and extend to the nature and type of therapy and therapist recommended in the guidance.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and

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					support plan without it affecting access to other aspects of their care.
National Council for Osteopathic Research	Guideline	026	009 - 011	Section 1.11.9 *Refer people with severe or very severe ME/CFS to a specialist ME/CFS physiotherapy or occupational therapy service for support on developing energy management plans.* We question the evidence to recommend only physiotherapy or occupational therapy services as other health care professionals could be equally trained and qualified to deliver specialist care. Might this be better stated simply as 'specialist ME/CFS therapists' which may include physiotherapists, occupational therapists, psychologists, osteopaths and or other health care professionals.	Thank you for your comment. The committee agreed that for people with ME/CFS it was important that the healthcare professionals with the appropriate clinical background and training supported any physical activity plans, here physiotherapist or occupational therapists.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 2 – People with severe MECFS	General	General	Our specialist therapy team acknowledge that there are a number of patients who suffer from severe CFS/ME and are not accessing specialist services. However the research presented in this document has a number of flaws. It was carried out using an online survey design, and instructions given were that carers, family members and even friends could complete the survey. The participants were self-diagnosed – what evidence did the researchers provide that the participants did indeed have CFS/ME, rather than another undiagnosed clinical cause for the fatigue? As NHS patients were not included, normal HRA approval did not need to be applied for. The researchers noted that the participants mentioned mental health difficulties but did not want to disclose them as they did not want to be dismissed. What evidence did the researchers therefore provide to say that these participants did not have mental health difficulties which were contributing towards their physical disabilities? 1/3rd of the participants had a gradual onset – a detailed clinical assessment may help to identify precipitating factors in such cases. Clinical experience indicates that gradual onset is often related to work-	Thank you for your comment. In Appendix 2, section 2.5.1 the study authors describe why they decided on an on line survey for this population. They also set out the limitations of the consultation, acknowledging there are limitations on using an online survey, on the recruitment and the representation of the sample. These include the points your raise about the survey and diagnosis. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making. *Ethics* Ethical approval for this project was granted by the University of Manchester Research Ethics Committee (2019-7763-12089)(see section 2.7 of Appendix 2) and conducted the study accordingly. The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS. People with severe ME/CFS were specifically identified by stakeholder as underrepresented in the published evidence. The study authors set out the limitations of the consultation acknowledging that patients who

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				related stress or ongoing emotional exhaustion from psychological events. Although this study may represent the views of a small number of patients who are members of patients groups, it cannot be generalised to the whole population of people with CFS/ME. Of note, at Page 10 line 37 it is stated that, 'many sufferers turn to online patient groups for support, disengage with traditional medical care and attempt to manage their condition without medical support.' The Strassheim et al (2018) study also recruited from a patient advocacy organisation and used charity organisations to advertise their study.	have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in this type of studies. This committee took this into account in the decision making.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 2 – People with severe MECFS	General	General	Additionally, clinical experience has demonstrated the presence of anger in the patient group towards staff. Clinical experience has also demonstrated the difficulties in engaging people with severe CFS/ME in rehabilitation. Our experience has indicated this is largely to do with most severe patients reporting being members of patient groups and having a negative view of the specialist teams before they come. It would be interesting to find out if the 9 who reported moving from moderate illness status to severe over the course of the illness held the belief that there was nothing they could do about their condition and also used the envelope theory, thus reducing their activity levels at the perception of an increase in symptoms.	Thank you for your comment.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 2 – People with severe MECFS	041	017	Researchers reported it is common practice in the ME community to rely on self-reports – this is certainly not the case in specialist services we do not rely on patient's testimonies until the relevant medical tests have been carried out. We would also	Thank you for your comment. When acknowledging this limitation, the research team are discussing this in the context of recruiting to a research project exploring the views of people with severe ME/CFS.

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				be interested to know what steps the researchers took when they identified participants where there were safeguarding issues. For example, people who had reported mental health difficulties, living alone with severe ME/CFS not accessing support from anywhere. Were these participants followed up and referred to local services?	Ethical approval for this project was granted by the University of Manchester Research Ethics Committee (2019-7763-12089)(see section 2.7 of Appendix 2) and conducted the study accordingly.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 3 – Expert Testimonies	General	General	We are unclear and uncomfortable about the use of expert testimonies to inform this guideline. What status have these been afforded compared with the other evidence considered? How were these experts chosen, and why so few of them?	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. *Choice of experts* Stakeholders during the scoping process and the committee in early meetings identified areas of the scope where there was a lack of evidence. Where this is the case additional evidence can be sought to support the committee in their decision making. There are several approaches that can be taken to provide the committee with additional evidence and these include calls for

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					evidence, expert testimonies, and in exceptional situations commissioned reports. See Developing NICE guidelines: the manual for further information on the process for including additional evidence (section 3.5 for expert witnesses). The ME/CFS methods chapter has details on the areas of scope selected by the committee for additional evidence. Three areas of the guideline were chosen for expert testimony, other areas were chosen for calls for evidence and for commissioned reports.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 3 – Expert Testimonies	General	General	We are particularly concerned by the testimony of Prof Edwards. He was asked to address the subject of 'The difficulties of conducting intervention trials for the treatment of ME/CFS'. In our opinion, he significantly over-reaches the scope of his brief. It would have been much more helpful to discuss the types of treatment modality that might be trialled in CFS/ME and what the gold standard trial design would be for those modalities. We are not convinced that Prof Edwards has the necessary expertise and knowledge in clinical trials of *non-pharmacological* interventions to make this assessment. For example, it is flawed logic to suppose that a trial of CBT or other psychological therapy should somehow attempt to separate the effect of the therapy *per se* from the effect of the therapeutic relationship. In real clinical practice, it is impossible to have one without the other, and a trial must reflect this reality. The criticism of many CFS/ME trials that they are based on flawed disease models is also grossly over-stated. We do not understand what causes CFS/ME, but this should not stop us from undertaking trials of possible treatments. If we have to wait for a complete mechanistic understanding of CFS/ME before we	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion. The committee acknowledged in his testimony the lack of existing objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures, which are methodological issues that are challenging for many areas of research not just ME/CFS. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations.

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				can do any trials, this does not help anyone, least of all the patients. Furthermore, even if a treatment is proposed based on a mechanistic understanding that subsequently proves to be flawed, this does not *de facto* invalidate the findings of the trial. It is entirely possible for a treatment to show benefit (or harm) that is mediated through a different mechanism that the one we expected.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Appendix 3 – Expert Testimonies	General	General	With reference to Professor Johnathan Edwards – he demonstrates, in his comments and arguments, a lack of understanding of the factors associated with a positive outcome of therapies, which include developing a personal relationship with caregivers. A positive, optimistic, and empathic relationship with therapists are shown to be important for a positive patient experience and outcome. Indeed, in the section above the committee reported on the detrimental effect on severe patients on having negative relationships with the NHS and the difference a positive relationship with their GP had. More specifically, he states: "The central difficulty for trial design in ME/CFS is the high risk of systematic expectation bias in a fluctuating condition with subjective core features". This is essentially true, but the same applies to mental health problems (fluctuating condition with subjective core features) where psychological treatments are considered valid options, yet the trials may share some similar design issues. If the committee are to take into account Professor's Edwards views on the role of subjective core features in a therapy based research trial, then they also need to take into account the	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion. The committee acknowledged in his testimony the lack of existing objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations. The committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic

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				subjective role of the qualitative studies they have claimed as 'evidence'.	considerations, resource impact and clinical and patient experience, equality considerations.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review A	General	General	An important topic, but we wonder whether this might have been broadened to look also at what information clinicians find to be most helpful for their patients to have. The evidence presented here had no control group. In general, there seem to be some findings about support and information which was received and reflected on as helpful.	Thank you for your comment. Evidence review B_ Information, education and support for health and social care professionals address explores what information health and social care professionals want to give people with ME/CFS and this confidence in doing this. This was a qualitative evidence review and the studies are not designed to have a control group.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review A	018	009	It is important we communicate to patients realistic goals depending on their own disability, not the disability of others. Individual plans help patients to achieve their realistic goals. It is important that we are as objective as possible with patients in terms of the amount of fatigue and disability that can be reduced.	Thank you for your comment. The committee agree and this is reflected in the recommendations on developing energy management plans and CBT. The committee recommend that people with ME/CFS are supported to choose realistic expectations and goals that are meaningful to them.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review A	029		I agree that patients who expressed confidence in their level of knowledge about CFS/ME tended to express less anxiety about the future. It is important that any NICE guidance and services can join such a patient in their hopefulness. Patients need to understand the complexity of the illness and medical/psychological testing will help to understand the complexities of the condition. Identifying factors that are maintaining the condition is a way out of the disability	Thank you for your comment. The committee agree that people with ME/CFS should be informed about their condition and this is reflected in recommendations on information and support. The recommendations reflect the complexity and variability of the ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review A	030	001 - 036	*Type of Evidence online* Most patients who use specialist services report that online information and ME groups have frightened them and many patients felt that online information from patient groups are 'all doom and gloom' and that Facebook Groups are all 'very angry' people. We would agree that NHS services would benefit from	Thank you for your comment. The committee agree that online information can be variable in quality and that it is important that NHS services should develop high quality realistic objective information for people with ME/CFS.

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				developing less biased information on the interventions for CFS/ME.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review A	039	009 - 046	*2.1 The quality of the evidence, and 2.2 Findings identified in the evidence synthesis* It is concerning that the committee placed so much importance on a systematic review that contained 15 relevant studies: all of them qualitative. While qualitative studies have a place in scientific research, such studies are 'used to understand people's beliefs, experiences, attitudes, behaviour, and interaction' (Vibha, Bijayini, & Sanjay, 2013). It is critical to understand the inherent issues with validity and reliability, as qualitative studies lack generalisability. Depending on the method used, qualitative studies may require as few as 6 to 8 participants in some cases. In the case of the systematic review in question, the number of participants across all the studies was 268. This creates a significant problem when we consider that CFS/ME patients are a heterogeneous group. While it is important to understand the experiences of CFS/ME service users, it is equally important to understand that the experience of a few service users is not a reflection of all service users in the UK. Furthermore, not all studies took place in the UK. Mihelicova (2016) was based on data collected from a book. Ryckeghem (2017) used Belgian participants, and Taylor (2005) used American participants.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). *Methods* The quality of the qualitative evidence has been assessed using GRADE-CERQual and this takes into account limitations, coherence, relevance and adequacy of the evidence. Mihelicova (2016) was rated as having serious limitations related to the use of public data due to lack of details on how the sample was derived, the methods of primary data collection and inability to assess bias. For this review it was considered that the information and support needs of people with ME/CFS is similar

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					across populations, for example wanting validation, information about the condition and their future. As noted above the quality of the evidence is one of the many factors taking into account by the committee when making recommendations. *Heterogenous population* Throughout the guideline the committee acknowledge that people with ME/CFS are a heterogenous population and the first recommendation raises awareness about how ME/CFS affects each person differently and the impact varies widely, from symptoms that allow people to carry on some activities to symptoms that can lead to substantial incapacity.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review B	General	General	Within the North of Tyne CFS/ME specialist team we are have constructed training packages for GPs, Medical assessors, mental health professionals, patient information on sleep, emotions, CBT, pacing, communicating with others, graded activity. These are all based on the evidence which has been rejected by the NICE 2021 committee. Therefore, we are at a loss to know what education we would be able to pass on to others. We would not support patients accessing information from ME organisations as we do not share the same model of CFS/ME.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).

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					Development of training materials Using these many sources of data and information the committee agreed that training should be developed by specialist services with input from people with ME/CFS and represent the experiences of all people with ME/CFS (see evidence review B). The committee agreed that ME/CFS specialist services can provide excellent information for both health and social care professionals and people with ME/CFS. As noted in an earlier comment made the committee agree it is important that NHS services should develop high quality realistic objective information for people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review C	006		Whilst it is the case that diagnosis does often take a long time, it is important to take into account the very nature of CFS/ME in that the symptoms are medically unexplained. For any condition to be medically unexplained, means that medical tests need to be carried out in an attempt to explain the presenting clinical picture. Due support needs to be given to the medical professionals who take these symptoms seriously and request an appropriate degree of diagnostic testing. Unfortunately, there are no short cuts to a thorough medical assessment. As mentioned earlier, around 50% of referrals to specialist CFS/ME medical assessors are considered to have another cause for fatigue.	Thank you for your comment. The experience of some of the committee members reflects your comment that 50% of referrals to specialist ME/CFS services are considered to have another cause for fatigue. The committee agree that it is important that people with ME/CFS have access to a timely and accurate diagnosis. The importance of undertaking investigations to exclude other diagnoses and seeking advice from appropriate specialists when there is uncertainty in interpreting signs and symptoms is emphasised in the recommendations in the section of the guideline on suspecting ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	049 - 052	006 (P49) - 036 (P52)	The committee discuss at length here and elsewhere why the IOM criteria are likely to be 'narrower' than some others (e.g. Fukuda) and therefore reduce over-diagnosis. This is simply supposition. There is no evidence presented which shows the level of agreement between these criteria. Furthermore, the authors seem to largely ignore the fact that the IOM criteria are the only diagnostic criteria set that does not explicitly require the exclusion of other causes of fatigue. This would therefore lead to	Thank you for your comment. *Comparison of the criteria* As you note the committee discuss at length the different diagnostic criteria (see committee discussion of evidence review D). In the report the level of agreement between the criteria is shown in table 4 where the symptoms in the criteria are compared side by side and section 1.2.31 lists the signs and

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				a significant risk of over-diagnosis using the IOM criteria. Drawing on my earlier point about seeking consensus between the published criteria (which also is the authors' justification for arriving at their proposed list of the core features of CFS/ME), it seems highly contradictory to ignore this one criterion (exclusion of other diagnoses) which features in all the sets of diagnostic criteria apart from the IOM. It is my experience that the core IOM criteria are indeed very characteristic of CFS/ME and thus helpful as part of the diagnostic process. However, that is not the same as saying that they are highly *specific* for CFS/ME, even when all features are present. There is a body of literature (some from our own centre) to suggest that what might be termed 'pathological fatigue', that is fatigue in the pattern of the IOM criteria, is also seen in some other medical conditions where fatigue is highly prevalent (for example certain neurological and autoimmune conditions). The authors then go on to present their own new set of diagnostic criteria by amending the IOM criteria. At the same time, they recommend that research is needed to better define the appropriate diagnostic criteria for CFS/ME. This seems contradictory. The committee are right to recommend further research and would do well to additionally make recommendations about how this should be conducted. They should not then undermine their own request for more research by nevertheless presenting a new set of criteria which are not supported by any research. They should instead make a recommendation along the lines of the following. *'There are several sets of published diagnostic criteria for CFS. None can*	symptoms common to the criteria and highlights where the difference are. *Differential diagnosis* The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.' The committee hope this adds clarity to these recommendations. Diagnostic criteria The committee agree that this guideline adds another set of consensus criteria and this is not ideal. The committee discussion in evidence review D sets out the committee's decision making, noting that it was important to give clear and informative guidance to assist clinicians, who may not be experts in ME/CFS, in identifying people with ME/CFS. Recognising that their recommended criteria are untested and this is an absence of validated diagnostic criteria they made a research recommendation to develop validated criteria. The committee agree with much of your suggestion (no gold standard, agreement and differences in the criteria, the use of clinical judgment and experience) and these are outlined in their discussion of the evidence however your suggestion that any published criteria could be used does not add clarity to the current situation in identifying people with ME/CFS and has not been added.

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				be considered as a gold standard. There is much agreement between these criteria but also some differences. This may mean that some patients would be classified as having CFS according to one set of criteria, but not by another. Until such a time as internationally agreed and validated diagnostic criteria are available, we recommend that clinicians use published criteria alongside clinical judgement and experience.'	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	028 - 029		IOM diagnostic criteria, whilst describing the 3 most common symptoms of CFS/ME, do not give any direction to primary or secondary care services on exclusion criteria. The risk, as mentioned above, is that patients who have other clinical causes of the fatigue will be diagnosed with CFS/ME. We note the committee has given the IOM an overall rating: serious limitations.	Thank you for your comment. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have made these edits and added: • examples of investigations to be done when suspecting ME/CFS • to the criteria when to suspect ME/CFS if the 'symptoms are not explained by another condition.' The committee hope this adds clarity to these recommendations. See evidence review D. Appendices D and E for how quality was assessed. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	007	028	Although delays have an impact on the physical and emotional health of persons – this is to do with intolerance of uncertainty. Patients frequently report that they would rather the tests they have come back as positive (even for say cancer), rather than them come back negative. The intolerance of uncertainty needs to be managed in primary care whilst patients are waiting for results. In order for the committee to recommend a diagnosis of CFS/ME at 6 weeks without an absolute requirement for medical tests to exclude other conditions, they would need to provide evidence comparing those patients at 6 weeks presentation who go on to be diagnosed with CFS/ME vs. another diagnosis (cancer, MS, thyroid disease, etc.).	Thank you for your comment. *Differential diagnosis* The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have made these edits and added: • examples of investigations to be done when suspecting ME/CFS • to the criteria when to suspect ME/CFS if the 'symptoms are not explained by another condition.' The committee hope this adds clarity to these recommendations. *Provisional diagnosis at 6 weeks*

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					To note 'Provisional' diagnosis has been deleted from the recommendations. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. Diagnosis is now introduced at 3 months.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	010	001 (Table 2)	The Fukuda diagnostic criteria were, and still are, the main diagnostic criteria used for research. When the NHS specialist teams were set up in 2005 we were required to use the Fukuda. It is illogical for the committee to decide 15 years later, and on a whim, that there has been a mistake in advising that Fukuda criteria be used in research and in NHS specialist teams. The Fukuda diagnostic criteria have very specific instructions on blood tests to be carried out in primary care and medical/psychological assessments to be carried out before a diagnosis can be made. The committee have argued that the Fukuda has very serious limitations because it does not use PEM as a required symptom. Clinical experience shows that over 90% of the patients seen within this specialist services report PEM and were diagnosed using the Fukuda. At the same time the committee needs to be aware that PEM is not highly specific to CFS/ME – patients who have numerous other medical conditions report PEM as a main disabling symptom.	Thank you for your comment. The committee disagree that the decision to update criteria that was recommended 15 years earlier is illogical and on a whim. The guideline was to update the NICE guideline CG53 published in 2007, this includes updating the evidence– in reference to the criteria the ICC and the IOM criteria were published in 2011 and 2015 respectively. It would have been an error to have excluded these criteria. *Fukuda criteria* See Evidence review D- diagnosis, the committee discussion section for the rationale why the committee considered the Fukuda criteria less appropriate for use in a clinical context in diagnosing ME/CFS. In particular see the section, 'development of criteria for research or clinical use' where the committee note that research criteria appear to be broader than criteria developed for clinical use. *Differential diagnosis* The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have made these edits and added:

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					• examples of investigations to be done when suspecting ME/CFS • to the criteria when to suspect ME/CFS if the 'symptoms are not explained by another condition.' The committee hope this adds clarity to these recommendations. *PEM* The Fukuda criteria does not include PEM as essential for the diagnosis of ME/CFS, and as a result if used by a non-specialist in ME/CFS people could be wrongly diagnosed with ME/CFS. This is a limitation, see evidence review D. Appendices D and E for how quality was assessed. *Diagnosis* The committee agree these symptoms in the criteria are seen in other conditions, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	048	006 - 025	This subsection is entitled 'the outcomes that matter most'; however, this issue is not actually addressed in this subsection. This subsection instead discusses the absence of a gold standard diagnostic test against which to compare the various available sets of diagnostic criteria. This is of course true. The committee then argue why this means that if two sets of diagnostic criteria differ, it is not possible to say which one is 'better' than the other. Again, this is true, in the sense of comparing their diagnostic validity. However, the committee do not then properly consider what would be the most appropriate reference standard in the absence of a gold standard test. I would suggest that the starting position for this would be to look for the areas of greatest commonalty between the various	Thank you for your comment. The committee disagree the rationale for the criteria is not adequality addressed. As you note the committee has at length discussed the differences and similarities between the criteria and the implications of these for a diagnosis of ME/CFS. These are set out in the benefits and harms, cost effectiveness and other factors the committee took into consideration sections of the committee discussion and interpretation of the evidence.

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				diagnostic criteria sets available. This exercise has in fact been undertaken and very clearly presented by the committee (Table 4), and yet this hardly seems to feature in the reasoning that follows when justifying the new diagnostic criteria which are then proposed in this guideline.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	048	026 - 039	In a similar way, the authors argue that in the absence of any gold standard against which to compare the validity of different diagnostic criteria sets, the appropriate 'next best' option is to consider the quality of the process by which those criteria sets were developed. We disagree with this. Quality of the guideline development process is of course important, but it is in no way a substitute for the absence of a gold standard reference test. Furthermore, the analysis of quality of the processes by which the various criteria sets were developed led to the finding that all had at least serious limitations. It is therefore inappropriate to make any further comparison of the relative merits of one set of diagnostic criteria over another. The committee should instead simply acknowledge that all the criteria sets had potential serious limitations in their development process.	Thank you for your comment. The committee agree that this is not a substitute for a gold standard but it is a reasonable method of evaluating quality of consensus criteria. See evidence review D. Appendices D and E for how quality was assessed and an explanation of the method used. In summary the AGREE II tool was used and we acknowledge that although this review does not include guidelines the principles of the decision making are similar in developing consensus based diagnostic criteria and it has been used the evaluation of consensus statements. While applying the AGREE II tool and assigning a score is less useful in this context the relevant items in the domains provide a robust set of principles to measure in the consensus criteria development. Table 11 in appendix D sets out the AGREE II domains and the relevant items evaluated in this review.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review D	057	014	Here, and elsewhere, the committee acknowledge the importance of excluding other conditions when making a diagnosis of CFS/ME. They also provide of a list of potential differential diagnoses in this section. Why then is 'exclusion of other causes of symptoms' not explicitly included in the proposed diagnostic criteria? Importantly, there is no mention of mental health disorders in this list of possible differential diagnoses. This seems a major oversight.	Thank you for your comment. The committee have revised the list of differential diagnosis in evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
Newcastle-upon-Tyne Hospitals NHS	Evidence Review D	058	023	This section discusses the relative merits of more or less stringent diagnostic criteria for enrolment of subjects into	Thank you for your comment.

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Foundation Trust				CFS/ME research trials. The committee go on to imply that the results of any CFS/ME trial which did not require the presence of PESE as an explicitly stated inclusion criterion cannot be considered applicable to any patients with CFS/ME. The committee use several instances of flawed logic in this section, as follows. • The committee suggest that use of 'broader' diagnostic criteria for enrolment in trials means that people who did not truly have CFS/ME will inevitably have been included in the trial. This argument is flawed because the committee have already acknowledged that there is no single gold standard for the diagnosis of CFS/ME. Therefore, all that can be justifiably said is something like the following. *'Interventional trials in CFS/ME have used different diagnostic criteria for enrolment. When considering whether the result of a trial may be applicable to a given patient, the clinician should consider whether they would have fulfilled the entry criteria for that trial.'* This approach is of course the one used in all branches of medicine. • Whilst not all sets of diagnostic criteria for CFS/ME have PESE as an absolute requirement, PESE (or an equivalent term) is acknowledged in specialist CFS/ME practice as being a very characteristic feature of CFS/ME. It is therefore highly likely that the vast majority of patients diagnosed with CFS/ME by whatever set of diagnostic criteria will have PESE. It is incorrect to assume that patients diagnosed with CFS/ME using criteria that do not include the presence of PESE as an absolute requirement will commonly lack PESE among their symptoms.	This section explains the problematic nature of defining the ME/CFS population and the differences in criteria developed for research or clinical use. The committee does not imply any trial which did not require the presence of PESE/PEM as an explicitly stated inclusion criterion cannot be considered applicable to any patients with ME/CFS. The committee agrees with your comment that the mix of criteria and the broader inclusion criteria of the research criteria has potentially resulted in heterogeneous study populations. As you also note trials in ME/CFS use different diagnostic criteria (potentially recruiting different populations) and this report (Evidence review D) illustrates and discusses in detail the differences in the criteria. This inevitably proposes some difficulties in interpreting the data and generalising the evidence that use different criteria. As you note PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *Further scrutiny of the evidence* *Based on the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further

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				- 'Broader' inclusion criteria for clinical trials inevitably increase the heterogeneity of the population of subjects enrolled. This will in turn increase variance in the outcome measures of interest and will make it *less* likely that a statistically significant effect will be detected. This general statistical principle runs contrary to what the committee are implying about the effects of overly broad inclusion criteria in CFS/ME trials. - In their review of diagnostic criteria for CFS/ME, the committee have proposed a new set of criteria. The validity of these proposed new criteria require validation by further research (as the authors acknowledge). It is therefore an outrageous jump from that position to suggesting that these proposed new criteria should be the standard by which all previous trials in CFS/ME should be judged! These trials generally used the set of diagnostic criteria for CFS/ME that was most prevalent at the time. This is entirely reasonable, and simply needs an acknowledgement about caution with generalising between studies that used different criteria.	scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review E	007	006	Introduction - A diagnosis of medically unexplained fatigue cannot be made until all medical tests indicated by the presenting symptoms have been completed – that is what medically unexplained means. Patients cannot expect anything other than a thorough medical and psychological assessment to identify any conditions were specific treatment is available. Patients need to be aware that large numbers of cases present to GPs with similar symptoms to CFS/ME and go on to be diagnosed with alternative conditions.	Thank you for your comment. The committee agree and have recommended that before ME/CFS is diagnosed it is important to carry out a thorough assessment, including physical and mental health and investigations to exclude other diagnoses. The committee recommend that ME/CFS specialist teams should confirm the diagnosis.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review E	007	011	The North of Tyne therapy team have produced a leaflet 'Living well with fatigue' that is handed out at the medical assessment appointment for patients awaiting outcome of medical tests.	Thank you for this information. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review E	015	005	It is important that patients are not given information about the ME patient community's understanding of a hypothetical 'energy envelope' at a time when patients may well be suffering from another medical condition that explains their physical symptoms.	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review E	015	031	Within the CBT model of CFS/ME – once a baseline is set and the patient understands their current energy capacity and keeping within this capacity – therapy would discourage patients from monitoring their symptoms. A fluctuation in energy levels and symptoms is 'normal' in everyday life for us all. When a patient knows they are working within their capacity, the CBT model helps them to challenge catastrophic thoughts about harming themselves if they stay within their capacity levels which they may have developed over several weeks. CBT uses activity sheets to monitor activity levels to help the patient understand if there is any particular reasons for symptom increase.	Thank you for your comment. This section refers to advice for people that are suspected to have ME/CFS and are acutely unwell. The use of CBT is not relevant here. The aim of this advice was to raise awareness that when people develop new or worsening symptoms they should return to their GP for advice. To make this clearer and reflect more accurately the recommendation the text in Evidence review E has been edited from 'monitoring' to 'being aware of changes in their symptoms'.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	005	011	The criticism comes from patient groups, and is NOT representative of all people with CFS/ME. Please see service evaluation table earlier in this document.	Thank you for your comment. This is the introduction to the review and provides a brief background to the topic.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	005	011	Pacing is an integral part of CBT and GET CBT.	Thank you for your comment. This is the introduction to the review and provides a brief background to the topic.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	005	012	This is a very outdated criticism of CBT by people who misunderstand the model – abnormal beliefs, behaviours and deconditioning are NOT seen as causative factors. The model suggests in SOME patients these can be understood as maintaining factors – individual assessment of patients is essential in identifying possible maintaining factors.	Thank you for your comment. This is the introduction to the review and provides a brief background to the topic.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	063	007	GET - The committee reinforced there is no therapy based on physical activity or exercise that is effective as a treatment or cure for CFS/ME. This challenges the evidence in the literature presented using the Fukuda criteria. Please see argument above.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the

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					committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as a therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories ofME/CFS, or that use fixed

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					incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	067	026	CBT is 'never' offered as a cure – following a CBT intervention some people are able to accept their fatigue levels – which are usually reduced from pre-morbid levels – acceptance of their condition reduces disability and allows people to engage in work and social life using less energy.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. From the qualitative evidence and the committee's own experience, they are aware of instances where some interventions, including CBT, are being misrepresented to people with ME/CFS and promoted as a cure for ME/CFS. Therefore, the committee agreed it was important to explicitly state that that there is no current treatment or cure for ME/CFS. The committee recognised that CBT can be helpful for some people, and this is reflected in the recommendations.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	067	027	CBT is not just supportive counselling - it requires patients to engage in strategies to reduce fatigue levels. This can be reduction in anxiety, relaxation, mindfulness, challenging negative beliefs about themselves which push them past their capacity. It is rather difficult to understand how the committee conclude the evidence for the efficacy of CBT and GET must be dismissed because they used the Fukuda diagnostic criteria; PEM is not a compulsory feature.	Thank you for your comment. *CBT* The committee agree that CBT is different to supportive counselling. Taking into account the range of stakeholder comments the recommendations on CBT are now under the sub heading cognitive behavioural therapy and psychological support has been removed reflecting that the recommendations are only about CBT. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). *PEM* The committee agreed that PEM was a key feature of ME/CFS and that people with PEM may react differently to interventions compared to people without PEM. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the

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					study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review G	221	001 (Table 80)	'Despite mixed pre-conceptions, most participants were positive about GET once they entered treatment.' This is also our clinical experience, and should be used to balance the negative opinions expressed elsewhere.	Thank you for your comment and information. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise

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					therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS,theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review H + Evidence Review I	General	General	There is ample evidence for successful strategies for the management of CFS/ME. The evidence base was confirmed by the NICE guidelines 2007 and was the basis for education and setting up of the specialist NHS services around 2005. The therapy team are aware of the contempt which is held by the patient groups regarding the management strategies that are used. However, the majority of patients who use the specialist services are very satisfied about the strategies that have previously been seen as 'evidence' based.	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what

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				It is not logical for the committee to dismiss this evidence because PEM was not a compulsory factor in the diagnosis. Clinical experience has shown that a very high percentage of patients who are diagnosed using the Fukuda diagnostic criteria present with PEM as a major feature. The committee would need to prove that the participants in the research trials frequently did not have PEM in order to reject this valuable research. Whilst our specialist team would have no objection to PEM being a compulsory symptom, as this is what we are seeing all of the time, we do not believe research should be rejected because Fukuda had PEM as a symptom that was not compulsory. Based on these views, the NICE committee's advice is going to make commissioning and re-commissioning of specialist services for people with CFS/ME exceedingly difficult.	recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). None of the evidence was dismissed and the committee discussions in Evidence reviews H and I detail how carefully the committee took into account all of the evidence on the management of ME/CFS. After considering the stakeholder comments the committee agreed to re-evaluate the evidence where studies clearly described PEM and the population with PEM was 95% or over (See evidence reviews G and H (appendix G) for the approach taken, the analysis and the impact on the results and interpretation of the evidence.). Throughout the guideline the importance of ME/CFS specialist services is reinforced and it is clear where access to these services is required. The management section of the guideline sets out the interventions for supporting people with ME/CFS to manage their symptoms, including if appropriate programmes for physical activity and exercise where specialist support is needed.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Evidence Review J	005	015	Our therapy team recommend that patients have the blood tests recommended by NICE 2007 at their GPs. They can then self-re-refer within 12 months, or after 12 months via their GP. Some patients are offered 3, 6, or 12 monthly reviews in the therapy team, depending upon patient needs.	Thank you for your comment and this information. The committee agree that some people with ME/CFS may require more regular reviews and the Review in primary care section of the guideline reflects this recommending people should be offered a review at least once a year.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	General	General	General	Overall, this draft guideline sets an extremely negative tone. There are several flaws in the reasoning that has been used to arrive at the recommendations, and the approach to synthesis of evidence seems often very unorthodox. The guidance seems to be written with only a subset of severe and refractory CFS/ME patients in mind, rather than the full breadth of the condition. As such, it simply does not fit with our own 15 years of clinical experience in CFS/ME.	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. *Evidence synthesis, decision making and strength of the recommendations* All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set

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					out the approach for the evidence synthesis before the data is collected. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	General	General	General	Throughout the draft guideline and supporting documents the committee has chosen to use the term 'ME/CFS', thus implying that this should now be the preferred name for the condition. We acknowledge that none of the currently available terms are entirely satisfactory, however we object to the way in which	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described*

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				ME/CFS places ME first. There is no evidence that the 'E' in ME actually exists. As a result, most specialists have moved away from the term ME. As such, 'CFS' is the most commonly used term, with CFS/ME considered as an acceptable alternative.	*using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	008 - 009	010 (P008) - 023 (P009)	The recommendation to suspect CFS/ME after 6 weeks of symptoms in adults (and 4 weeks in children and young people) is problematic, especially when combined with the concept of 'making a provisional diagnosis of ME/CFS'. Whilst having the symptoms suggested (box 1) for 6 weeks/4 weeks cannot be considered as 'normal', it is not unusual for these kinds of symptoms to be present for 6-12 weeks in post-viral fatigue and during recovery after severe illness. This is especially the case after COVID. A distinction must therefore be drawn between a GP *considering* a diagnosis of CFS/ME, vs. '*making a provisional diagnosis*'. In our centre, about 50% of patients referred from primary care for specialist assessment turn out to have a diagnosis other than CFS/ME. It is our overwhelming experience that once a label of 'possible CFS/ME' is given, this is very hard to undo. This often results in considerable challenges for the specialist team and distress for the patient. I would instead suggest that GPs are advised to consider further investigation of fatigue if it is of more	Thank you for your comment. *Suspecting ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence section of evidence review D. The committee note in the rationale for suspecting ME/CFS that it is also the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted that the advice recommended at this stage would not be detrimental to people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has

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				the 6 weeks duration, particularly when associated with the other features in box 1. At this stage in the diagnostic pathway, the patient might be considered as having symptoms of 'excessive fatigue', but *not* a provisional diagnosis of CFS/ME. There is no adequate scientific or clinical justification given for the proposal to reduce the timeline required for making a diagnosis of CFS/ME to 6 (or 4 in CYP) weeks for provisional and 12 weeks for confirmed diagnosis. The guideline authors acknowledge that these recommendations are shorter than any of the international criteria that were reviewed in producing this guideline. The authors justify this change by saying that most patients with CFS/ME experience delays in diagnosis which are often distressing and potentially associated with worsening of their condition. It is of course true that many patients with CFS/ME do experience delays in their diagnosis, but it is a gross oversimplification to assume that this can be solved by reducing the minimum symptom duration for diagnosis. Whilst the cardinal features described in box 1 are very typical of CFS/ME, they are far from being the only symptoms. As the authors acknowledge, there are many other possible symptoms, affecting many organ systems. Patients very frequently present with combinations of multiple physical symptoms which can be very challenging to unpick. It is relatively unusual that a patient presents to primary care with clear-cut CFS/ME. Inevitably, this is likely to require multiple consultations in primary care and potentially specialist opinions from secondary care. This process inevitably takes time, and indeed it is often only after repeated clinical assessment that the diagnosis of CFS/ME becomes	addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. As you note this combination of symptoms cannot be considered normal and should be investigated but the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. As you note people with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started

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				clear. Given the lack of any diagnostic test for CFS/ME, it is all the more important that the initial clinical assessment is done thoroughly and carefully. It is true that many patients who ultimately are diagnosed with CFS/ME do have multiple cycles of consultations with specialists and investigations before the diagnosis of CFS/ME is finally made. In many cases, there is potential scope to prevent unnecessary referrals and over-investigation by earlier suspicion of CFS/ME and earlier referral to a specialist CFS/ME service, but a balance needs to be struck with a safe minimal level of investigation. The concept of reducing minimum symptom duration relies heavily on the wisdom of hindsight. Most patients ultimately diagnosed with CFS/ME will indeed agree that the diagnosis might have been made earlier. However, this discounts that other group of patients who initially presented with similar symptoms, but ultimately turned out to have another diagnosis. In our service, even with a mandatory minimum investigation set in primary care, and careful triage of referrals, about 50% of those patients seen in our service with suspected CFS/ME turn out to have another cause for their symptoms.	at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. COVID-19 To note the guideline was developed before the COVID-19 pandemic.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	024 - 025	006 (P024) - 003 (P025)	What is the evidence for energy management? What is the evidence for the hypothetical 'energy envelope'? How does a person know the boundaries of their envelope if they have been scared by reading these proposed NICE guidelines and are afraid of their symptoms or of making themselves relapse? These are the kinds of catastrophic thoughts that patients bring to specialist services after reading this kind of information.	Thank you for your comment, Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have

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					while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity (see Evidence review G for the committee discussion on self-management strategies). After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	055 - 056	023 (P055) - 006 (P056)	The rationale for the recommendations on safeguarding is concerning – although people with CFS/ME commonly report that they are not believed, this is not a reason to ignore standards in safeguarding practice, as this guideline seems to suggest. Furthermore, this sections identifies that there is no evidence on safeguarding in CFS/ME so logically the safeguarding approach should be the same as for any patient group where there is not specific evidence to justify divergence from normal practice. We question the "consensus" approach taken in this guidance as it is not supported by our local team or discussions with our national colleagues on this topic – is there a skewed perspective on the topic in this consensus?	Thank you for your comment. Safegaurding was discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of

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					symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	004	020	This line should more appropriately read, *'Some people who are members of ME support groups or Facebook groups for ME do not wish to engage with health and social care as they hold the belief that ME is an incurable illness with no treatment.'* Some people living with CFS/ME feel angry with NHS specialist services, and with the offer of therapy that is based on evidence from research trials. These specialist services offer interventions that reduce symptoms in some people with CFS/ME, and in others, provide considerable relief from symptoms allowing patients to engage more fully in their work, social and family life. In support of this experience, please see below outcome results from our North of Tyne Specialist therapy service. These results are in complete contrast to the tone set by NICE throughout their draft guideline document. The current tone of the draft NICE guidelines, without a contrasting reference to the evidence of those patients who have chosen to access specialist services and have engaged in CBT or GET, will further discourage patients to engage in these specialist therapies. Ethically, NICE needs to present a balanced view so that patients can make fully informed decisions regarding their potential options for treatment. Results of North of Tyne CFS/ME patients service evaluation	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and the impact it has had. It is based on the evidence identified in the Evidence reviews A and C, Appendices 1 and 2, and the committee's experience. The current wording reflects the evidence. *Tone of the guideline* After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations included the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.).

Question		2016 n

Would you recommend the service to others?	Yes	100%	92%	93.5%	98%
	No	-	8%	6.5%	2%
Was the service beneficial to you?	Yes	85.7	89%	93.5%	98%
	No	6.1%	11%	6.5%	2%
If you needed to seek help in the future would you return to service?	Yes	94%	89%	93.5	96%
	No	-	8%	6.5%	4%

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	005	020 - 026	We do not dispute that prejudice and disbelief is the experience of some CYP with CFS/ME, but the guideline may have over-emphasised this and appears to suggest that this is the norm.	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience. The current wording addresses this.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	005	010	Needs to be clarified. As mentioned in the guidance, patients present with several symptoms which need to be medically assessed thoroughly before a confident diagnosis of CFS/ME can be made. In our service, about 50% of patients referred by GPs with suspected CFS/ME had other conditions which explained the fatigue and were hence not sent on to the therapy team for assessment/intervention. Although these additional tests may take time, they are crucial to ensure safe practice.	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity. The committee have experience of people being referred to ME/CFS specialist services and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. The committee have now included examples of investigations that might be carried out.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	005	018	In the North of Tyne service, when patients are discharged they are given 12 months in which they can self-re-refer. After 12 months, the patient's GP can re-refer directly to the therapy team (without the need for further medical assessment) with	Thank you for your comment and information.

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				confirmation that the blood tests recommended by NICE 2007 have been completed and continue to be in the normal range.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	005	019	There is a lack of recognition in this guideline that children and adults are not the same. The differences between the two groups are not emphasised, nor the specific issues for adolescents and those transitioning between paediatric and adult services.	Thank you for your comment. The committee agree that children are not the same as adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	006	001 - 006	Although parents do act as the advocate of their CYP, it is necessary to place more emphasis on the need for direct engagement with CYP as there are safeguarding concerns if the voice of CYP is lost (if it is recommended that parents can speak for them).	Thank you for your comment. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	007	001	It is no clear that there is sufficient evidence of a *need* for a low stimulus environment, rather than a *preference* for one. This can be a circular symptom in that patients from the severe end of the spectrum spend time in isolation with no stimulation – having stimulation is a challenge to every part of their system. If the patient wanted to engage in therapy, we would recommend a very gradual increase in stimuli - so gradual that the system does not recognise the increase.	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these difficulties and the support that may be needed to manage their symptoms.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	007	0 22	How to best assess the risk from an interaction problematic if this is wholly based on potential for temporary worsening of symptoms. Interaction is needed for progress – there must be an allowable discomfort. A better choice of words might be, 'risk of prompting a flare or relapse'.	Thank you for your comment. 'Worsening their symptoms' is an example of what may happen as a result of an interaction and that this should be assessed. As an example there is no judgment on the whether an interaction that has an impact on symptoms is discouraged. This decision would be a result of discussing the risks and benefits of interactions with the person with ME/CFS**.**

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	008	003 - 004	Needs to add: '…including the exclusion of other conditions which would be reasonably expected to have brought on these symptoms.'	Thank you for your comment. In the criteria for suspecting ME/CFS,' and symptoms are not explained by another condition' has been added.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	008	005	There is no clear guidance given as to the minimum set of investigations required to exclude other diagnoses. Whilst no guidance could hope to cover every possible cause of fatigue, it is relatively straightforward to propose a minimum set of blood tests that should be done in primary care as part of the initial workup for possible CFS. Such an approach reflects current UK practice, and it is unclear why this is not recommended in the draft.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	008	012	What is the evidence for 'minimum 6 weeks in adults and 4 weeks in children and young people'? 6 weeks/4 weeks is far too soon to be considering a diagnosis of CFS/ME – there may be a variety of reasons why a person has not fully recovered from post-viral fatigue within this time span, for example. Additionally, not all patients have a readily definable / abrupt onset of CFS/ME symptoms (for example following a viral infection) - some patients have a gradual onset. There will be a number of patients presenting with the 4 proposed cardinal symptoms of <4-6 weeks duration in primary care who will get a false positive diagnosis of CFS/ME. This may then influence the behaviour of both the patient and the GP in terms of decision making around further medical assessment.	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms at this point are given advice that may prevent them getting worse. In summary it would be unusual for an acute illness, including a viral illness to persist longer than this with all the symptoms. The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has

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				This could have serious implications for patients who do get a false positive diagnosis of CFS/ME.	addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	008	017	The use of the term 'fatigability' is problematic. Fatigability has a rather specific and limited definition as a clinical examination finding in neurology practice. The adoption of this term to better describe the fatigue experienced in CFS/ME is therefore potentially confusing to medical practitioners who are less familiar with CFS/ME.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change fatigability. This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by

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					activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' The committee hope this has added some clarity for readers.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	009	021 - 023	Of course this would affect a provisional diagnosis – and this should be explained very clearly to patients if given a 'provisional diagnosis' of CFS/ME. As this diagnosis may need to be withdrawn, it would be better not to use the term in the first place.	Thank you for your comment. The committee disagree if the diagnosis is withdrawn they then won't have a suspected diagnosis of ME/CFS but while people have a suspected diagnosis of ME/CFS they should follow the advice in section 1.3.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	009	017	There is simply no evidence to support this position. There is an implicit assumption that reducing minimum symptom duration for diagnosis is a risk-free strategy. This is based on the assumption that the approaches recommended for the management of *established* CFS/ME are likely to also be helpful in early cases of *suspected* CFS/ME. Whilst it is certainly possible that early intervention with a CFS/ME model of care might be helpful, it is also entirely possible that it might be harmful. For example, telling a patient that they are very likely to have a life-changing chronic illness after only 6 weeks of symptoms may have a profound effect on their physical and mental well-being. The new guidance should instead simply recommend that, 'research is needed to define optimal early management of suspected CFS/ME'.	Thank you for your comment. This recommendation was to ensure that clinicians were alerted to the possibility of ME/CFS as soon as possible. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected

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					ME/CFS could be give advice without the need to be told they have a provisional diagnosis The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	009	017	As the stigma associated with this diagnosis has already been noted, why would we give the 'provisional diagnosis' sooner than is necessary? It is entirely possible and reasonable to give general fatigue symptom management advice without needing to make a provisional diagnosis. The intolerance of uncertainty is the factor which makes waiting for results difficult – this applies to all patients in the NHS who are waiting for results – not just patients who have CFS/ME.	Thank you for your comment. This recommendation was to ensure that clinicians were alerted to the possibility of ME/CFS as soon as possible. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This

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					section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	010	002	Please pluralise to specialists - not just fatigue specialists - what else may cause these symptoms?	Thank you for your comment. Appropriate specialist here does refer to expertise in supporting the interpretation of signs and symptoms where there is uncertainty and a possible alternative diagnosis. Throughout the guideline where a specialist refers to a ME/CFS specialist this has been made clearer by including ME/CFS before specialist.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	010	017	What does, 'not use more energy than they perceive they have' mean? Is there good evidence that patient perception of their available energy matches reality? How is a patient able to accurately judge this? This question is frequently asked by patients in the clinic, and takes time and experience to establish.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of trial evidence to support advice for people with suspected ME/CFS and this includes energy management. However the committee agreed the advice would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about

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					managing their energy and how much rest is appropriate for the individual.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	010	018	The use of boundaries as conceptualised in an 'energy envelope' can create anxiety in a patient and a fear of making their symptoms worse by activity. It is our experience that the limits of the 'energy envelope' are often underestimated by patients. What is the evidence for the existence of an 'energy envelope', and how do patients measure this? Surely, this is the same concept as setting a 'baseline' in traditional CBT and GET. The concept of an 'energy envelope' is vague at best – but problematic – envelopes are static - there is no sense of them being something that can change size and shape. The concept also does not appear to allow for activities which can increase energy levels, e.g. eating, rest, sleep etc. The notion of an 'energy envelope' implies there are both upper and *lower* bounds to the amount of energy that should be expended by a person. However the tone of the advice presented in this section of the draft guidance really refers only to the avoidance of expending excessive energy (i.e. crossing the upper bound of the envelope). What about the avoidance of expending too little energy (crossing the lower bound of the envelope). This is equally important in the management of CFS/ME. As mentioned above, the concept of establishing a personal 'baseline' is probably more helpful here.	Thank you for your comment The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of trial evidence to support advice for people with suspected ME/CFS and this includes energy management. However the committee agreed the advice would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about managing their energy and how much rest is appropriate for the individual. After considering the stakeholder comments the committee agreed that the concept of an energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
Newcastle-upon-Tyne Hospitals NHS	Guideline	010	020	Rest, in itself, will not ameliorate CFS/ME. It needs to be incorporated in a management plan. Rest is of course necessary	Thank you for your comment.

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Foundation Trust				for patients with CFS/ME, but this also has to be managed, for example interspersed with small amounts of paced activity to prevent/minimise deconditioning. Excessive rest otherwise also risk harm in the longer term.	The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term before diagnosis. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this would not cause harm to anyone.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	011	006	Add, 'after exclusion of other relevant potential diagnoses'.	Thank you for your comment. 'and other conditions have been excluded.' has been added to the recommendation.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	011	007	It is not clear whether the committee expect the diagnosis of CFS/ME to usually be made in primary care or in the specialist clinic setting. My reading of the guidance is that (for adults) it is expected that usually the diagnosis would be made in primary care and the patient be referred to a specialist CFS/ME team for management. For the same reasons as outlined above regarding 'suspecting ME/CFS', I think this is an unsatisfactory approach, which grossly trivialises the difficulty of making a secure diagnosis of CFS/ME in many patients. Experience and confidence with CFS/ME varies widely between GPs. Whilst increased education of GPs and other health professionals about CFS/ME is of course desirable, it is not realistic to think that a confident diagnosis of CFS/ME can be made in primary care in most cases. Making a diagnosis of	Thank you for your comment. The evidence and the committee experience reflect your comments about the lack of confidence in GPs in diagnosing ME/CFS (see evidence reviews B, D and I). The committee agreed it was not clear in the recommendations about when a diagnosis is made and after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for a diagnosis for both the clinician 'provisionally diagnosing' and the person with the symptoms. • It has been clarified that if symptoms continue for 3 months then a person should be referred to a ME/CFS specialist team for confirmation of the diagnosis and development of

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				CFS/ME requires very careful consideration of all the available information and a detailed assessment of the patient. In many clinics, including our own, an initial medical assessment in a specialist CFS/ME service takes about an hour of consultation time, along with additional time for a careful review of previous medical records. There will then be a further lengthy assessment by the CFS/ME MDT. Primary care in the UK is simply not configured for this kind of level of assessment. GPs rightly expect that this will be done in the specialist CFS/ME service. This should be made explicit in the guidance. It is also important to remind patients, ME groups and primary care workers that some co-morbidities will exclude a diagnosis of CFS/ME.	the care and support plan. It is at this point a detailed assessment is then recommended. This is set out in Section 1.5 Assessment and care planning by a ME/CFS specialist care team.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	011	009	There are a lack of specialist services for CYP with a diagnosis of CFS/ME and this is not recognised in this guideline, nor is there any recognition of national referral pathways.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams.
Newcastle-upon-Tyne Hospitals NHS	Guideline	012	007	In specialist services, we commonly see patients with dietary issues. These may be due to vomit phobia, choking phobia, 'fad' diets, or diets with intensive supplement usage. Interventions	Thank you for your comment and information. The section on dietary management and strategies provides further information on dietary strategies.

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Foundation Trust				would be directed at the maintenance of a 'healthy diet', which can sometimes markedly reduce physical symptoms. Anorexia nervosa and Bulimia will cause physical symptoms which overlap with CFS/ME, and therefore need to be assessed for and excluded.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	014	016	It is unethical to frighten patients with the implication that CFS/ME is inevitably fluctuating in symptom severity. Whilst fluctuation is a feature of CFS/ME it can usually be managed with appropriate specialist care. Fear of fluctuation can create an anxiety response in patients who have not had specialist CFS/ME care, and such patients report that they worry that their symptoms are going to deteriorate. Activity management and the use of activity schedules completed by patients help them to identify factors that can influence the changes in symptom levels therefore patients can learn to manage their condition and feel like they have more control of the symptoms.	Thank you for your comment. The committee disagree, it is accepted that ME/CFS does impact people differently and there is a wide range of impact in how its affects people's lives. This is supported by the qualitative evidence in evidence reviews A and B and their experience for this reason your suggested edit has not been made.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	014	019	This comment is unduly negative and has potential to produce significant anxiety in patients. The comment about it being less common to have longer periods of remission may apply to those patients with severe CFS/ME, but is not the case for the mild to moderate patients. When patients learn to manage their condition, the physical symptoms reduce and do not necessarily come back. We question why the emphasis should be on the negative end of the spectrum.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	014	019	The fluctuating nature of CFS/ME is usually linked to boom-and-bust activity cycling and can be identified using activity recordings. This gives a patient the sense of control over their fatigue levels and there is less of an emphasis of unpredictability.	Thank you for your comment and information.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	014	028	It is misleading to say that the condition itself is necessarily worsened by infections. Patients may feel more poorly or more fatigued during the infection, but it is important that patients understand that the additional symptoms are linked to the virus causing the current infection, and generally reduce to the previous baseline once the virus is out of their system. Although anecdotal, it is our clinical experience that childbirth per se does not cause a worsening of CFS/ME, and most of our patients who get pregnant do well.	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples as suggested in your comment were considered potentially misleading information and not always a trigger and there are comments that gave other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	015	001	This point should be emphasized more strongly, as this guideline is overly negative in tone and does not reflect the much better outcomes in the paediatric population compared with the adult population. Without this, the guideline will give an incorrect and skewed picture to CYP and their families.	Thank you for your comment. After considering the stakeholder comments the committee agreed to delete the word usually.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	015	004	It is important that appointments are attended as specialist services are a scarce resource – we offer telephone calls and now video calls as alternative. If the patient can't attend it is important, they contact the service with a telephone call or ask their support person to telephone on their behalf – the responsibility is two way	Thank you for your comment. The committee agree the care is best delivered collaboratively.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	015	006	Many CFS/ME patients who use specialist services report negative experiences of self-help groups. They are frightened by their members negativity, and their belief that they can never improve.	Thank you for your comment. This recommendation was supported by the evidence and the committee's experience (Evidence review Information for people with ME/CFS for further information).
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	015	015	Most patients who attend specialist services do not find ME support groups supportive	Thank you for your comment. This recommendation was supported by the evidence and the committee's experience (Evidence review Information for people with ME/CFS for further information).

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	016	005 - 008	It is concerning that the tone of section 1.7 in general, and the CYP section in particular is at odds with usual safeguarding practice. It is enshrined in safeguarding practice in adult and paediatric settings that safeguarding is not the role of experts, but of everyone who has input into the life of the CYP or adult in question (for example, https://www.rcpch.ac.uk/resources/child-protection-external-guidance). The tone of the current guideline will work against this well-recognised strategy to improve safety and needs to be adjusted.	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. With regard to Safegaurding the importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	016	009 - 011	It is important that patients understand energy balancing when they return to work or education – energy balancing so that they are aware of activities or copying strategies that use/waste energy. For example, many patients report working at a 120%	Thank you for your comment. The section on managing ME/CFS includes information on energy management.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				level management plans are developed to look at ways of adjusting to a less perfectionist level of functioning.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	016	009 - 011	This is a very concerning way of phrasing this statement. Symptoms of CFS/ME are not "confused" with signs of abuse or neglect, rather there may be symptoms in common between CFS/ME and abuse and neglect. To suggest that health professionals may be confused about symptoms and signs that may point towards a safeguarding issue is deeply worrying. We should be ensuring that any concerns are appropriately discussed and escalated, involving the child, young person or adult in question, their MDT and wider context. To not do this risks that cases of abuse or neglect that may appear to be CFS/ME on the surface are missed, that family members that are the agents of the abuse or neglect are not identified, and that direct harm is caused to this group of children, young people and adults by this guideline. NICE should not be condoning this in any way.	Thank you for your comment. The importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	017	008 - 019	As per the point above, the language use here is very concerning. The phrase "…are not necessarily a sign of abuse or neglect" in lines 8-9 should be revised to emphasise that the points in lines 11-19 can be signs of abuse and neglect, but may also be present in CYP with confirmed or suspected CFS/ME in families where abuse and neglect are not present.	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.

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					The following recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	018	015	But vice versa is also true, and should be considered/ explored (sensitively) prior to confirmation of diagnosis of CFS/ ME.	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to edit the recommendation. The reference to it might be a fear has been removed.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	021	003 - 010	This section is only presenting the negative possibilities – this section should start with a statement about the fact that many individuals with CFS/ME (and most CYP in particular) are able to continue in work, education or training despite their diagnosis, and that there are many benefits to this to individuals and families (and the wider society). However, some people do find that an unstructured approach to these contexts can worsen symptoms.	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	021	001 - 002	This section (1.9) does not provide enough information about the value of school to CYP beyond the educational aspects. Evidence has been submitted to NICE separately via the Young People's Health Special Interest Group of the RCPCH from our local Young Person's Advisory Group North England (YPAGne).	Thank you for your comment. The committee agree that the value of school can go beyond education and further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion.

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				YPAGne highlighted on their review of these guidelines that they lack an appreciation of the extra value of the school environment to CYP. This has been made more widely apparent to all during the COVID-19 restrictions in 2020. YPAGne members reflected that their experience of lock down in COVID-19 had many parallels with the experience of CYP living with confirmed or suspected CFS/ME. Quotes from YPAGne members to illustrate this: "Social aspects- seeing friends but also support for higher education e.g. Uni. Without school, you wouldn't have the support to apply or the skills needed to do well there," "the social side of school and life as a young person was completely dismissed and that work or school has more to it than just work".	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	022	003 - 005	Also need to include information about the CFS/ME MDT service advising on reasonable adjustments to exams and assessments in line with the individual's current needs and capabilities.	Thank you for your comment. This is included in the earlier recommendations in this section.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	023	016 - 020	There needs to be more information on the specific issues regarding transition of care from children's to adults' services – for example the issues around education and higher education and additional support for this requires careful management.	Thank you for your comment. The NICE guideline linked to on transition from children's to adults' services has more information.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	024	004	It is our opinion that it is unethical for NICE to recommend informing patients with CFS/ME that there is no current treatment or cure, non-pharmacological or pharmacological. The committee need to understand that this sets up feelings of hopelessness and helplessness, which are barriers to engaging with specialist services. 15 years of clinical experience indicates that some people are 'cured', others live quite effectively managing their fatigue levels, and most improve in ways that are important to them.	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. However while the committee agree there are people who recover there isn't currently a cure for ME/CFS and it is important

<table>
<tr><th>Stakeholder</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments</th><th>Developer’s response</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>that people with ME/CFS are aware of this. For this reason, the committee have not further edited the recommendation.</td></tr>
<tr><td>Newcastle-upon-Tyne Hospitals NHS Foundation Trust</td><td>Guideline</td><td>024</td><td>004</td><td>Please read the following extract from the North of Tyne CFS/ME 2019 service evaluation.

What has changed for you as a result of attending the service?
<table>
<tr><td>THEME</td><td>EXAMPLES</td></tr>
<tr><td>Management of Condition and Symptoms</td><td>“Control over condition and understanding of how t
“I can deal with my symptoms more easily than bef
“I now fully understand my condition. The affect it
with it.”
“how I live with and manage with my limited energy
coping techniques and help on how to cope better
of this illness”
“Managing my condition better. I’ve learnt to pace
on myself”</td></tr>
</table></td><td>Thank you for your comment.

To note after considering the stakeholder comments on the wording ‘treatment or cure for ME/CFS’ the committee agreed to remove the word ‘treatment’ from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.</td></tr>
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				Acceptance and Adjustment to Condition	"I have an acceptance of my condition and a positivity to make the best of it and to not let it rule my life but to try and push myself a bit more each day but accept bad days too" "Relaxation techniques change my perception of my expectations of life with CFS/ME"	9 comments (12.68%) From 7 people (14.58%)	
				Improved Mental Wellbeing	"My quality of life has improved dramatically" "I have a much more fulfilling life and am better able to nurture myself" "My mental health has improved a great deal" "It has enabled me to live my life as fully as possible"	14 comments (19.72%) From 13 people (27.08%)	
				Sense of Validation	"Feel validated that I am coping with a recognised condition that deserves attention in order to function at my best"	4 comments (5.63%) From 4 people (8.33%)	
				Reduction of Fatigue	"My fatigue levels improved during my time with the service. This has allowed me to do more in my daily life"	3 comments (4.23%) From 3 people	

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				Unclassified | "I have returned to work (albeit in a reduced capaci work : life balance" "Aware of places that can help me in future (not jus 1 person reported that nothing has changed. The wording of the draft guidance in this section seems to imply an extremely narrow concept of 'treatment', along the lines of it being 'a therapy which results in complete and permanent remission of all symptoms of CFS/ME by targeting a biological pathway that is accepted to be the cause of CFS/ME'. The real meaning of treatment is surely any therapy which 'lessens the severity of one or more symptoms of CFS/ME and/or increases functional capacity despite the continued presence of such symptoms'. By simple analogy, analgesia for a patient with pain due to terminal cancer is an appropriate 'treatment' even though it does not cure the cancer.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	024	021	This is basically a good description of true graded exercise therapy when properly performed. The PACE trial was only one version of GET, which (unnecessarily in our opinion) tried to artificially separate GET from pacing.	Thank you for your comment. The committee recognised that although graded exercise therapy is not recommended it was important that people with ME/CFS have access to a ME/CFS specialist team to provide support with physical activity and exercise programmes where appropriate. The committee have recommended that a physical activity or exercise programme may be offered to people with ME/CFS who feel ready to progress their physical activity beyond their current activities or who would like to incorporate physical activity or

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					exercise into the managing their ME/CFS. Such a programme should start by establishing a physical activity baseline at a level that does not worsen symptoms, initially reducing physical activity to be below this baseline level, which should be successfully maintained for a period of time before any attempt to increase it. Flexible adjustments should then be discussed, agreed and made to a person's physical activity. To accompany this the committee have made recommendations that set out how strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that use are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS'
Newcastle-upon-Tyne Hospitals NHS	Guideline	025	003	Deconditioning may not be the cause of CFS/ME, but this statement risks also implying that there no role for deconditioning	Thank you for your comment.

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Foundation Trust				in CFS/ME. Any person who is inactive will become deconditioned – it is hard to understand why someone with CFS/ME will not also become deconditioned if they spend long periods inactive.	After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	025	018	We need to be careful here – many patients have already reduced their activity to almost zero before attending clinic. In reality, the first step should be to ensure a stable, paced baseline, which *might* need to include a reduction in activity.	Thank you for your comment. After considering the range of stakeholder comments this was edited to 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	025	025	It is important to acknowledge that symptoms can also be triggered by emotional distress and stress, not just by excessive physical activity. In this scenario, a reduction in physical activity will not reduce symptoms, and there comes a very real danger of reducing activity to a point when people are doing less and less in an attempt to improve. It is important that patients gain an understanding of triggers of their flare-ups so that they can reduce the energy around the triggers. Some triggers are inevitable, and rest will not prevent patients needing to manage potential triggers. In a similar vein, we have concerns that provisional diagnoses of CFS/ME are given to patients in primary care before a specialist CFS/ME psychological wellbeing assessment to identify whether debilitating fatigability is caused by excessive cognitive or	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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				emotional exertion. Experience shows that it can take varying amount of time to identify the significance of these factors on fatigue.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	026	016	The guideline committee need to be aware these recommendations for physical maintenance are also exercises, and the only way to bring these safely into a management plan would be through true graded exercise under specialist supervision.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. In addition, 'Include strategies to maintain and prevent deterioration of physical functioning and mobility in the care and support plans for people with ME/CFS. Strategies may need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the care and support plan and the priorities and symptoms that people may have.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	027	021	A clearer distinction should be made between physical activity in general, and physical activity supervised by specialist services. Clinical experience has demonstrated that some patients believe that activity management in specialist services is harmful too which then affects engagement in the therapy which will reduce symptoms of fatigue.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and

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					specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	027	023	We need to be careful not to imply that a worsening of symptoms (hurt) is necessarily wrong or the same as a deterioration in health (harm). Should this clause also state that we should advise patients not to do these activities? It is the need for structure and supervision that is key here.	Thank you for your comment. After considering the stakeholder comments this has been edited to,,' do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.'
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	028	006 - 007	GET as administered by most specialists is NOT based on fixed incremental increases - this was a characteristic of GET within the PACE protocol only.	Thank you for your comment. The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise

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					or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	028	008 - 009	There is no such thing as an exercise programme based on deconditioning being the cause' it is just an exercise programme – cause or effect is irrelevant. In the therapy team, we have seen patients who have received a CFS/ME diagnosis or provisional diagnosis benefit from engaging in structured activity based on deconditioning as a *maintaining* factor, but never seen as *causal*. We have never received any feedback stating that this has been harmful in the patient service evaluation described earlier.	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise avoidance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS .
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	028	010 - 011	What is meant by, 'therapy derived from osteopathy, life coaching and NLP'? If this refers to the Lightening process, then just explicitly say that. There are other therapies that can have value if used properly.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	028	021	Why has NICE emphasised the negative responses of a limited number of patients? There is no need to emphasise that some people have found that physical activity can make their symptoms worse. It is important that we share realistic hope for patients. Being cautiously optimistic is valued by patients. What NICE is not emphasising is that many people also report that they found resting for too long actually makes their symptoms worse. Why has NICE emphasised the negative rather than the positive first? Clinical experience has shown that this negative emphasis for some people make them very anxious about doing anything. Experience has linked fluctuation in symptoms to 'boom and bust' activity cycling. Boom and bust has not been mentioned at all in these guidelines which seems very surprising as it is an absolutely cardinal feature of patients with untreated CFS/ME.	Thank you for your comment. This point was to illustrate that the impact of a physical activity or exercise programme can vary. The committee recognise that there are many different terms used in the ME/CFS community. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the commissioned report on children and young people) and their own experience. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. After considering the stakeholder comments the committee agreed to clarify that, 'energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).' It is now clearer that this avoids the 'boom and bust' pattern.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	028	027	Why does this recommend to, 'start by reducing'? Setting a baseline is evidence based – what is the evidence base for setting an energy envelope?	Thank you for your comment. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. This is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly. To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	030	013	Managing pain – there is far more to managing persistent pain than is suggested here, and far more guidelines are available. It is incorrect to suggest that pain in CFS/ME is only neuropathic or headache. Pain is a core feature of CFS/ME in many (but not all) patients, and tends to be experienced out of proportion to expectations. It should therefore be considered as part of the holistic management of CFS/ME, rather than as a separate issue as is implied here by the reference to other guidelines.	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee agree that care for people with ME/CFS should be personalised and recommend a personalised care and support plan in the assessment and care planning section of the guideline. Management of pain should be part of the personalised plan. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy

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					management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	034	005	Clinical evidence is that people with CFS/ME can recover using the CBT model – in helping them to understand why they engage in boom-and-bust activity cycling. This understanding helps them to resist engaging in activity levels above their capacity on good days, thus preventing busting, and the psychological sequelae of the fear of relapse. CBT is not merely a 'supportive therapy' – whilst as psychological therapists we hope we are 'supportive' – engaging in CBT therapy involves commitment and the acceptance that changing behavioural patterns and the negative view of self will reduce fatigue levels. CBT can reduce physical symptoms associated with insomnia, anxiety and depression which are often attributed to CFS/ME. Clinical experience demonstrates that it can be 'curative' although CBT is never offered as a 'curative' therapy, and the experienced specialist therapist will offer cautious optimism. With most therapies, pharmacological or non-pharmacological, some	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.

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				patients benefit, and some do not. Some patients have side effects, and some do not. A pharmacological therapy is not withdrawn if clinical trials have indicated its effectiveness in a clinically significant number of patients. No therapy is ever offered as being 100% effective.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	034	011	What are the risks of CBT in CFS/ME? What is the evidence for these risks? Is it qualitative evidence?	Thank you for your comment. It is good practice to discuss the risks and benefits of any intervention and CBT is no exception. This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks for the person and able to ensure the person with ME/CFS makes an informed choice.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	034	016	Clinical experience has demonstrated that when patients 'believe' there is no cure, and 'believe' there is no possible improvement in the future, they become hopeless and even suicidal. Clinical experience has demonstrated that these are indeed 'abnormal' illness beliefs. These beliefs are NEVER considered as causative of CFS/ME – but again as one of the possible maintaining factors.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness.

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					The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	036	005	A distinction should be made between being alert to the possibility of coexisting conditions in CFS/ME that may need specific treatment, vs. the presence of medical or psychological conditions which would exclude a diagnosis of CFS/ME.	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. After considering the stakeholder comments the committee have now included examples of investigations that might be carried out. In addition a recommendation on assessing new symptoms has been added to the review in primary care section of the guideline to reflect this. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	036	007	Almost all diagnostic criteria for CFS/ME exclude medical conditions which share the same symptoms as CFS/ME this makes absolutely sure that physical symptoms are not dismissed by the medical assessor if it is considered to be linked to a clinical cause rather than CFS/ME. For example, thyroid disease and coeliac disease may share the same symptoms as CFS/ME and hence if untreated, would exclude the diagnosis of CFS/ME.	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. After considering the stakeholder comments the committee have now included examples of investigations that might be carried out. In addition a recommendation on assessing new symptoms has been added to the review in primary care section of the guideline to reflect this.

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					Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	036	012	The guidelines should acknowledge here that particular challenges of mood disorders in the context of CFS/ME. The physical symptoms of anxiety include*: dry mouth, rapid breathing, rapid heart rate or palpitations, fuzzy head, feeling faint, headaches, muscle tension, restlessness, sickness, loose bowel movements, loss of appetite, going to the toilet frequently, difficulties getting to sleep, feeling hot or cold, sweaty or clammy, feeling disconnected from things.* These symptoms show considerable overlap with CFS/ME. Physical symptoms of anxiety may be missed by prematurely diagnosing CFS/ME, which may prevent patients from receiving treatment to reduce these physical symptoms. A diagnosis of significant anxiety would exclude a diagnosis of CFS/ME. Similarly, the physical symptoms of depression include: *headaches, back pain, muscle aches and joint pain, chest pain, digestive problems, exhaustion and fatigue, sleeping problems, change in appetite or weight resulting in weight gain or loss, dizziness or lightheadedness, and loss of libido.* The same argument applies as above for anxiety.	Thank you for your comment. This section links to the NICE guidance on co-existing conditions and does not any detail about the overlap of symptoms. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	040	011	It would be interesting to know what NICE now considers to be 'current knowledge in ME/CFS'. The NICE guidelines 2007 (and their supporting evidence base) would have been seen by most professionals working in CFS/ME as being a good reflection of the current knowledge in the field. However, these have been very largely dismissed in these draft 2021 guidelines.	Thank you for your comment. The first recommendation in this section has been edited to, 'health and social care providers should ensure that all staff delivering care to people with ME/CFS maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. '.

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					The committee note that the NICE guidelines 2007 were published 14 years ago and the evidence base has developed in that time.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	040	017	Given the dismissal of the majority of the existing evidence base for CFS/ME in these draft guidelines, it is unclear what this 'evidence-based content' would be. Are we to assume the evidence base is the qualitative studies referred to in the guidelines?	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The first recommendation in this section has been edited to, 'health and social care providers should ensure that all staff delivering care to people with ME/CFS maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. '.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	042		Omission - No definition is given for Graded Exercise Therapy.	Thank you for your comment. A definition has been added.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	045	017	Unrefreshing sleep is not the same as 'light sleep'. This does not fit with our clinical experience – many patients describe a long, deep sleep, but feeling unrefreshed on waking.	Thank you for your comment. After considering the stakeholder comments, this definition has been edited to,' Unrefreshing sleep means that is non-restorative. Even after a full night's sleep people do not feel refreshed. People with ME/CFS often report waking up exhausted and feeling as if they have not slept at all, no matter how long they were asleep.' to aid further clarity.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	006 - 009	Just because there is no biomedical test available for CFS/ME, this does not leave the condition without a diagnostic process. It is entirely unclear why the committee felt that they 'could not give a list of standard tests'. Whilst clinical judgement will of course be required, it should be relatively straightforward to provide a minimum set of diagnostic tests, as indeed is current NHS practice. Services were set up nationally in the England using the Fukuda criteria, which are very specific about what tests need to be carried out to confirm a diagnosis. Vague statements like this lead patients into a hopeless state. It is not clear that the committee understands a normal diagnostic process and how diagnostic uncertainty is normally managed. Until suitable baseline tests have been carried out, this should most definitely affect a provisional diagnosis of CFS/ME. If we were to use the same logic that is being proposed for CFS/ME, is every patient who has trouble swallowing going to be given a provisional diagnosed of esophageal cancer? For some patients	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. In addition the committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'.

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				who have been extremely anxious about a possible diagnosis of cancer it is very difficult for them to believe the tests were negative. It is therefore illogical to make a clinical diagnosis of CFS/ME (whether provisional or not) without the benefit of baseline tests.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	010	The ME/CFS community need to acknowledge the value of the diagnostic testing that is currently being used by specialist services and ensures that patients receive a thorough medical assessment before a diagnosis is made.	Thank you for your comment. The Committee agree and they have experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	014	The is no sound justification for the committee's belief they can simply adapt the IOM diagnostic criteria in order to produce a wholly new set of criteria which simply align better with their own opinions.	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to

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					interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would be no need for the committee to address this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS. The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion. The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce the number of misdiagnoses through allowing short-lived fatigue to be

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					excluded. The committee emphasised the importance of identifying and excluding other conditions, and that these should be appropriately investigated in people with suspected ME/CFS. **The committee also made a research recommendation to validate the consensus criteria.**
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	016	Post Exertional Symptom Exacerbation / Post Exertional Malaise is indeed a symptom that is reported by just about all of the patients seen in specialist services who are diagnosed using the Fukuda criteria. There is no sense is which Fukuda excludes PEM, as is implied here. To discount Fukuda, the committee would need to show clear evidence that patients without PEM are frequently being diagnosed with CFS/ME. This is simply not our clinical experience.	Thank you for your comment *PEM, indirectness and relevance* As you note PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The Fukuda criteria does not have PEM as an essential criterion. The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	021	Does the committee have the authority to decide to 'revise' a criteria?	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If

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					there was an agreed set of criteria there would have been no need for the committee to address this question.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	049	024	The committee appear to simply rely on own their experience, presumably of people who have been diagnosed with CFS/ME, that 6 weeks can safely be used as a minimum symptom duration, contrary to all existing guidance. The committee present no evidence for those who have persistent symptoms 6 weeks after a virus and went on to be diagnosed with another medical condition.	**Thank you for your comment.** After considering the stakeholder comments including those on the risk of early diagnostic labelling, the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are that provisional' diagnosis has been deleted. The committee agreed that the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	050	005 - 011	We agreed with the committee that the non-specific nature and common presentation of some CFS/ME symptoms make it difficult to diagnosis and distinguish from other conditions. The specialist teams are therefore guided by the Fukuda criteria, which clearly set out the other conditions that need to be explored when considering an alternative diagnosis.	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses

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					and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	050	021 - 025	The Fukuda diagnostic criteria give clear direction to primary care staff on the blood tests that are required before referral to specialist services. If these criteria are not used there will be a definite increase in the number of patients who receive a diagnosis of CFS/ME. The committee have not adequately considered what safeguards should be put in place to prevent delayed referrals to appropriate services for the patients who will receive a false positive CFS/ME diagnosis. The burden of referral onto alternative specialist services will lie with medical assessors in specialist services. Waiting lists for CFS/ME medical assessment will increase putting patients with alternative conditions at risk of delayed potentially lifesaving treatment. The committee do not appear to fully appreciate what a major change in approach they are advocating. Before the committee act on this, they should do a scoping exercise with primary care	Thank you for your comment. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. • Further investigation/differential diagnoses. The committee have similar experience of people being referred and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought. The

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				in order to identify the number of patients experiencing the proposed 4 cardinal symptoms (debilitating fatigue, post exertional symptom exacerbation, unrefreshing sleep and cognitive difficulties) in an average GP clinic.	committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	050	005	Debilitating fatigue, post exertional symptom exacerbation, unrefreshing sleep and cognitive difficulties are NOT symptoms that are sufficiently specific to distinguish CFS/ME from other conditions at a 6-week stage.	Thank you for your comment. The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in Evidence review D-Diagnosis. The committee agree these symptoms are seen in other conditions particularly fatigue, but note it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	050	019	It is suggested that the proposed guidance will 'standardise practice' in the face of a current 'mix and match' approach. However, it is our understanding that when specialist services were set up in the NHS they were based on using the Fukuda diagnostic criteria. There is therefore already a 'standardised approach' in place. Staff in specialist services take symptoms seriously and appropriately use clinical experience alongside standardised criteria.	Thank you for your comment.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	052	004 - 014	It is unclear why the ME/CFS community's opinion appears to take precedence over the research evidence base. When used in a specialist service, the Fukuda criteria are not broad. It is our clinical experience that the combination of medical tests and psychological assessment can accurately identify people with and without CFS/ME as well as is possible, in the absence of a diagnostic test.	Thank you for your comment. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria and the assessments recommended in the guideline.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	052	030	The IOM criteria are not 'stricter', as (uniquely among the available criteria) they do not detail the medical and psychological assessments that need to take place. Making a diagnosis of CFS/ME in anyone who has these symptoms is unsafe and unethical.	Thank you for your comment. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria and the assessments recommended in the guideline.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	053	003	The idea that earlier advice and care could prevent progression contradicts the view presented elsewhere in the draft guideline that there is no treatment that improves the course of CFS/ME.	Thank you for your comment. *Treatment and cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations and to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	053	008	It is stated that having a personalised management plan is key to 'managing ME/CFS symptoms successfully'. Does this mean that a management plan prevents disease progression and disability? If so, this seems to run counter to the opinions expressed elsewhere in the guidance about the irreversible nature of CFS/ME. Where is the evidence for this?	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The care and support plan would include detail on any strategies for managing ME/CFS or treatments for managing symptoms.
Newcastle-upon-Tyne Hospitals NHS	Guideline	054	025	What are considered to be 'accurate' expectations about the future? This is difficult to predict with any accuracy at an earlier	Thank you for your comment. The rationale reflects the evidence that people with ME/CFS reported that they valued being given realistic information about

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Foundation Trust				point in the illness. Furthermore, the outlook itself may depend significantly on the approach taken by the specialist team at this stage. Should the patient be told there is no cure, no treatment and a general lack of evidence? Or should they be met by an optimistic specialist team that has the skills and knowledge based on research trials that will help them to progress in coping with their condition?	ME/CFS to enable them to think about their future. This often came from sources such as, ME/CFS specialist teams and support groups (see evidence review A). Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	055	005	Clinical experience has shown that patients who engage with specialist services find the negative attitude of local and national support groups too difficult to cope with early on in their CFS/ME journey. Some patients have described support groups as all doom and gloom, focusing on how ill people are, some patients have described them as a 'pity party'. As such, we have found that in some cases these support groups are indeed harmful to the patient. Within specialist services, we acknowledge the disability and loss, but then focus on what can be done to reduce the level of distress or disability.	Thank you for your comment. The rationale reflects the evidence that people with ME/CFS reported that they valued being given realistic information about ME/CFS to enable them to think about their future. This often came from sources such as, ME/CFS specialist teams and support groups (see evidence review A). Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	059	013	It is very difficult to image that specialist services are going to be developed in under-served areas of the country when the committee have emphasised that there are currently no diagnostic criteria, and no treatment plans other than rest and the 'energy envelope' theory. Specialist services would not be deemed as necessary to give this very limited advice. In making their draft recommendations, the committee have rejected the existing model of NHS care for people with CFS/ME. Therefore there is no longer a model to present to	Thank you for your comment. After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS.

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				commissioners for re-commissioning of existing services and commissioning of new.	To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs and access to specialist services to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	060	004	There is considerable evidence for CBT and GET. The committee has chosen to dismiss this evidence based on a lack of PEM as a specified inclusion criterion. The committee needs to recognise that their approach risks dismantling specialist services and patient care will be adversely affected.	Thank you for your comment. No study was excluded because recruitment did not include PEM as an essential criterion. The *PEM* The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *CBT*

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					Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and

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					application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	060	007	Whilst it is agreed that some unscrupulous persons are offering 'cures' for CFS/ME at considerable cost to patients, it is considered offensive that the specialist NHS CFS/ME services set up in 2005 which have offered considerable support and interventions appear to be included in the same category.	Thank you for your comment. This paragraph does not refer to specialist NHS CFS/ME services it refers to people offering cures for ME/CFS where there is often a financial cost to people with ME/CFS when they pursue these. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	060	010	The committee fail to acknowledge the national set of outcome measurers which were agreed before the setup of specialist teams in 2004: Chalder Fatigue, HADS, pain scale, Self-Efficacy scale, SF36, Epworth sleepiness scale.	Thank you for your comment. This refers to the development of core outcomes sets for research, to date one for ME/CFS has not been developed. See https://www.comet-initiative.org/
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	060	025	We do not recognise the basis for the 'controversy over GET'. Where does the evidence of harm from GET come from? In 15 years working as a specialist team, we have not met any patients who were harmed by GET. Who offered these patients graded exercise therapy? What is the evidence that a relapse was down to exercise therapy and not another variable? Clinical experience has demonstrated the boom and bust pattern, which is prominent in patients seen in specialist teams, is usually the cause of flare-ups. GET sets a low baseline and some patients find it very difficult to maintain their activity levels at a low baseline. They may engage in activity cycling which is against the GET model of care. Therapy should be aimed at helping the patient resist the boom and bust activity cycling. This does not eliminate the role of GET altogether.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach

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					taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of chronic fatigue syndrome . These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F

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					and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. There was concern, particularly from the lay members of the committee, about the wording of CBT manuals that make suppositions about 'wrong' cognitions. The committee considered that the narrative around fear avoidance and false illness beliefs can deny patient experience, as fears can be completely rational and protective against harm. Therefore, the committee decided to specify in the recommendations that CBT does not assume people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of ME/CFS, but recognises thoughts, feelings, behaviours and physiology and how they interact with each other.(See evidence reviews G and H for the evidence and the committee discussion on these recommendations). This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. After considering the stakeholder comments the committee agreed to clarify that, 'energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability

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					or downwards when symptoms are worse).' It is now clearer that this avoids the 'boom and bust' pattern.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	061	007 - 008	'The key component is … the 'energy envelope'. There is no evidence for an 'energy envelope' so how can this be justified as the key component of a plan. As discussed above, we advise that establishing a 'baseline' is more appropriate.	Thank you for your comment. The concept of energy limits and the balancing of energy expenditure is a common tool used in ME/CFS. Baseline is used in the energy management section as the lower end of the limit. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	061	016	As discussed earlier, we are concerned about the use to the term 'harm'. If muscles that have not been used for a while are activated, there may be a physical response, which need not be defined as 'harm'.	Thank you for your comment. Harm refers here to people with severe or very severe ME/CFS experiencing further deterioration in their symptoms and condition.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	061	020	Standard 24 hour 7 days a week activity schedules are used as part of GET and CBT and used in specialist services. We also use step counters as most patients have a device for monitoring these and patients have reported they are either surprised at how little or how much they are doing.	Thank you for your comment and information.
Newcastle-upon-Tyne Hospitals NHS	Guideline	063	002	The committee is over emphasizing the 'harm' caused as reported in some of the qualitative evidence. Qualitative evidence is not a suitable tool to determine 'harm' from an intervention. Harm needs to be proved by objective tests.	Thank you for your comment. Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses

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Foundation Trust					the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. When developing the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. People with ME/CFS reported harms in the qualitative evidence. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Guideline	063	007	The committee needs to be honest open and transparent with patients by acknowledging that there is evidence for the efficacy of therapy based on physical activity and exercise, but they have chosen to discount this evidence based on a technicality. Some	Thank you for your comment. No study was excluded because recruitment did not include PEM as an essential criterion. The PEM

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				people do 'recover' following GET, but GET is never offered as a 'cure'.	The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a

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					chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased

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					perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Newcastle-upon-Tyne Hospitals NHS	Guideline	064	008	Fuller discussion is needed, both of the role of sleep disturbance in CFS/ME, and the potential for primary sleep disorders to mimic	Thank you for your comment.

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Foundation Trust				CFS/ME. For example, the physical symptoms of insomnia include: *aching muscles, confusion, memory lapses or loss, depression, hallucinations, hand tremor, headaches, malaise, styes, sensitivity to cold, bags under the eyes, increased blood pressure, increased stress hormone levels, increased risk of diabetes, increased risk of fibromyalgia, irritability, obesity, and yawning.* There is clearly considerable overlap with the symptoms CFS/ME. Sleep hygiene is not a 'cure' or 'treatment' for CFS/ME. However, clinical experience has demonstrated that once sleep difficulties are identified, sleep hygiene reduces the 'symptom load' of those symptoms that are related to insomnia.	After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Question from comments form	1		1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. The proposed changes to the diagnostic criteria for CFS/ME are likely to result in very significant impact on practice. In particular, the combination of reduced minimum symptom duration for suspected diagnosis, combined with the proposed use of diagnostic criteria that do not explicitly require exclusion of other causes of fatigue, represent very major departures from most currently accepted UK practice. Furthermore, the requirement for symptoms to have a 'specific onset' (1.2.3) risks missing that subgroup of patients with CFS/ME who have a gradual symptom onset. These changes will present challenges to primary care (increased workload from early referrals, lack of clear guidance as to the extent of investigations needed in primary care) and for specialist services (a greater proportion of patients being referred	Thank you for your comment and information. In response to stakeholder feedback, the committee have now removed reference to a provisional diagnosis and a specific onset. They have made recommendations about testing for alternative conditions. Therefore, the demand on services should not be so great and the recommendations easier to implement. The diagnostic criteria are slightly stricter than in the previous guideline, although the duration of symptoms in adults has been reduced by one month to be consistent with children. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of

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				who require further investigation and/or monitoring before a diagnosis of CFS/ME may be confidently made or rejected). The North of Tyne CFS/ME therapy specialist services has been in operation since 2005. We pride ourselves on offering evidence based medical and psychological assessment based on the Fukuda diagnostic criteria, and evidence based treatment based on research trials and NICE 2007 guidance. We have been able to successfully reduce distress and disability in many of our service users by using this evidence base. If implemented in its current form, the draft NICE 2021 guidance would strip specialist CFS/ME services of this evidence base, and the specialist experience that has built up over 15 years of practice. This would be replaced by a set of personal opinions and beliefs derived from some members of the ME community, as outlined in the NICE 2021 committee's guidelines. Therefore, if the draft NICE 2021 guidance is implemented in its current form, specialist CFS/ME therapy services will lack structure and direction. This will have a negative effect on patients' outcomes. It will also present serious challenges in the commissioning of specialist CFS/ME services, as they will have been deemed to have no evidence base. This in turn will have a detrimental effect on the recruitment and retention of therapist staff. If the draft NICE guidelines 2021 are adopted in their entirety they will prove difficult or impossible to implement. The NICE committee have presented a naïve and skewed belief about the	the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence from studies that were based on the use of the CDC/Fukuda diagnostic criteria were not dismissed but were downgraded, reflecting a common criticism that those criteria are too broad. The guideline continues to recommend CBT and the wording of this recommendation is now less negative in tone. In conclusion, the committee have modified some of its recommendations in response to stakeholder feedback. They assert that this guideline is based on the broad evidence base and are confident that commissioners will demand these services.

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				lack of evidence for interventions for CFS/ME, by dismissing research evidence from studies that were based on the use of the CDC/Fukuda diagnostic criteria. Presenting a skewed picture of CFS/ME, a lack of operationally useful diagnostic criteria, and a lack of evidence for appropriate interventions, will make it significantly less likely that commissioners will continue to fund existing specialist CFS/ME services, and highly unlikely that they would commission services in areas of the country where such specialist services do not already exist.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Question from comments form	2		2. Would implementation of any of the draft recommendations have significant cost implications? The proposed move to a six-week minimum duration of symptoms for suspected CFS/ME would potentially result in the referral of increased numbers of patients who have fatigue that would naturally improve or resolve if observed for a little longer. This would have cost implications for primary care or for specialist services, depending on the commissioning position. If the draft NICE recommendations of giving a provisional diagnosis at 6 weeks are adopted, there will be a significant number of false positive diagnoses of CFS/ME. The 4 cardinal symptoms proposed in the draft guidance are NOT wholly specific to CFS/ME patients. The committee has not considered the detrimental impact of a lack of appropriate medical tests being performed on patients who do not have CFS/ME but nevertheless have these 4 cardinal symptoms. The apparent belief of the guidelines committee in the specificity of these criteria demonstrates a naivety in their understanding of the number of patients with other 'clinical causes' who have these 4	Thank you for your comment and information. The earlier referral might have a resource impact although if patients' symptoms go away then the referral can be cancelled while they are on the waiting list. The committee have responded to stakeholder feedback by adding recommendations on testing for and excluding other conditions. However, the committee also note that post-exertional malaise, as defined in this guideline tends to be more significant than the post-exertional malaise observed in other conditions. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need commissioning and investment, such as provision of care for severe and very severe ME/CFS costs, The committee agrees that video consultation technology will be important, although for the initial assessment, the committee stressed the importance of a face-to-face consultation. This guideline highlights areas where resources should be focussed and those interventions that should not be

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				symptoms, present to primary care practitioners, and go on to be diagnosed with another medical condition. Whilst the committee are attempting to address the delay in diagnosis of CFS/ME, in so doing, they are creating problems in other areas of the care pathway. There would be significant cost implications for both primary and secondary care services if more patients were to be referred with a diagnosis of CFS/ME. If appropriate medical tests are not considered in primary care, they will instead need to be considered by the experienced CFS/ME medical assessors. This would mean that more medical time in specialist CFS/ME services is spent in assessing patients and carrying out the appropriate medical tests or referring on to other appropriate specialist services for further assessment. Many of these investigations could have been requested in primary care to exclude other diagnosis, as indeed they are at present. Furthermore, more therapist time will be spent assessing and offering management plans to patients with fatigue of very recent onset, whose condition may well naturally improve with time. This would be a waste of specialist medical and therapist time, and represent an unnecessary extra cost to the health economy. Furthermore, very early (provisional) diagnosis of CFS/ME risks an early 'pathologising' of symptoms, which may be clinically unhelpful for those patients whose symptoms would resolve spontaneous, or would be more appropriately managed by other medical specialists. Many centres (including our own) are not set up or funded to perform home visits for those with severe or very severe CFS.	recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				This would require specific commissioning. It may be that video consultation technology can help get round this challenge.	
Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Question from comments form	3		3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) Primary care providers will require much clearer advice on when to refer patients with suspected CFS/ME and what investigations to do prior to referral. In our locality, we currently have a largely successful system requiring GPs to perform a number of tests to exclude other common medical causes of fatigue (in line with the previous NICE guidance) before the patient is referred to the specialist service. The North of Tyne CFS/ME therapy team's existing pathway is an example of good practice, which uses the Fukuda diagnostic criteria to exclude clinical causes of fatigue and uses evidence-based practice.	Thank you for your response. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme.
NICE – Quality and Leadership team	Guideline	004	General	Section 1.1 - It would be difficult to draft a quality statement from some of the recommendations in the 'principles of care' section as many of these recommendations are 'be aware' or 'recognise'.	Thank you for your comment. The committee recognise these recommendations are hard to measure but they were keen to ensure that the guideline included recommendations that highlighted and corrected some of the key misunderstandings about ME/CFS.
NICE – Quality and Leadership team	Guideline	008	010	Section 1.2 - Rec 1.2.3 says 'suspect' ME/CFS however recommendation 1.2.6 refers to 'their provisional diagnosis'. Can recommendation 1.2.3 be amended to state that people are given a provisional diagnosis if they have the symptoms listed? Alternatively, as suspected ME/CFS is used frequently in the guideline, could a recommendation be included to clarify that people with suspected ME/CFS are given a provisional diagnosis? This will help to ensure that people with suspected ME/CFS are given a provisional diagnosis promptly and it would also help with any quality standard development in this area.	Thank you for your comment. After considering the stakeholder comments on the risks of early diagnostic labelling recommendation 1.2.6 has been edited to remove 'provisional diagnosis'. This recommendation does refer and link to the diagnostic criteria.

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NICE – Quality and Leadership team	Guideline	010	General	Section 1.3 - As above, it would be helpful if it was made clearer that section 1.3 is for people who have a provisional diagnosis of ME/CFS. Adding a recommendation to section 1.2 would cover this.	Thank you for your comment. The section title is Advice for people with suspected ME/CFS and both recommendations have suspected ME/CFS in the stem.
NICE – Quality and Leadership team	Guideline	013	012	Section 1.5 - Rec 1.5.5 - This recommends home visits for people with severe ME/CFS which may not be possible during / post-pandemic though we appreciate this would be the most appropriate type of appointment for this population. Could the recommendation also note that where this isn't possible appointments could be by telephone / video as suggested in recommendation 1.8.1?	Thank you for your comment. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the assessment and development of the care and support plan but other methods may be more appropriate depending on the person's symptoms.
NICE – Quality and Leadership team	Guideline	072	022 – 023	It is noted that the 'context' section of the guideline states that there is unequal access to specialist services across England and Wales.	Thank you for your comment.
North Bristol NHS Trust - CFS/ME Service	Appendix 3 - Expert testimonies	General	General	It is not clear why the expert testimony were included from Professor Jonathan Edwards. It is clear that Prof Edwards' expertise is in pharmacological research, and not in research into non-pharmacological interventions. It would have been more useful to have an expert witness who understood the issues related to non-pharmacological interventions rather than one who focussed primarily on the problem on non-blinding. At one point (page 6) he criticises studies which do not show objective improvements and then immediately criticises the studies which did show objective improvements: "Some exercise studies show objective changes in indices of fitness but that does not necessarily imply a reduction in illness or disability", domains which are typically assessed using subjective measures. The impression is of someone who wants to have his cake and eat it.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence . Stakeholders during the scoping process and the committee in early meetings identified areas of the scope where there was a lack of evidence. Where this is the case additional evidence can be sought to support the committee in their decision making. There are several approaches that can be taken to provide the committee with additional evidence and these include calls for

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				Prof Edwards states that "*unblinded trials with subjective outcomes* are specifically considered unreliable." If NICE as an organisation were to generalise this opinion across all guidelines for example those for back pain, osteoarthritis and multiple sclerosis, what would the impact of this opinion be on these other guidelines? Prof Edwards puts forward the idea that placebo is due to "positive thinking" but does not seem to acknowledge the biological element of placebo, and the element associated with training. It would be advisable to find an expert who could offer a more informed view of non-pharmacological issues, rather than one whose expertise is in a different field.	evidence, expert testimonies, and in exceptional situations commissioned reports. See Developing NICE guidelines: the manual for further information on the process for including additional evidence (section 3.5 for expert witnesses). This guideline included 3 expert testimonies. Professor Edwards was invited to provide his expertise on some of the methodological controversies in undertaking research in his area. The committee acknowledged in his testimony the lack of objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures, as you note in your comment these are methodological issues that are challenging for many areas of research. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence.
North Bristol NHS Trust - CFS/ME Service	Guideline	005	019	Additional principles for those in work (We suggest something about this is added in p 7 as section 1.1.12) Heath professionals should be aware that a large proportion of people with ME/CFS will be struggling with work, or become unable to work. Questions about work, including travel to work will elicit the nature of the challenge. For those in work, the management plan needs to account for this and additional support and resources may be required. For financial and other reasons, work may be the main priority to the detriment of other areas. Emotional support as well as support in making practical changes at work may be required. Research suggests that difficulties with work will not be improved on unless they are addressed explicitly. Occupational Therapists can offer expertise in this area of self-management.	Thank you for your comment. Section 1.9 Supporting people with ME/CFS in work and education address how people can be supported at work and further information has been added into the committee discussion in evidence review A.

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North Bristol NHS Trust - CFS/ME Service	Guideline	010	021	We suggest the addition of advice to maintain a sleep routine	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support more detailed recommendations on rest and sleep in people with suspected ME/CFS, but they agreed the advice on rest would not be harmful in the short term before diagnosis. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this would not cause harm to anyone. Section 1.12 recommendations on rest and sleep management are for people that have been diagnosed with ME/CFS and as such are more detailed.
North Bristol NHS Trust - CFS/ME Service	Guideline	012 013	010 - 012 009 - 010	We suggest that the management plan can be more holistic and include the patient's goals and values. In this context, the health professional is facilitative not directive. The plan can then be reviewed within the with the therapist after a period of time where not only the achievements or challenges are discussed but what has been learnt, how this experience can relate to other areas of self-management, and what other resources may help. A management plan like this can be entirely operated by the patient (and their family if appropriate). The therapists' role is to elicit the values and help the individual identify their roles, then support, encourage guide, and help with setting realistic goals. Challenges in achieving goals can be seen as learning points and in the process, goals may need to be entirely changed. The patient is in control of this at all times and the health professional	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) This approach supports personalised care and support planning where a plan is developed after an initial holistic assessment.

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				considers how the service can support them. This input could be varied but may include regular phone or video calls; outpatient appointments; being part of a group that supports and reflects on this process of self-management.	
North Bristol NHS Trust - CFS/ME Service	Guideline	012	010	We suggest that the word "collaborative" is included in this line, for example "Collaboratively develop a personalised management plan…"	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
North Bristol NHS Trust - CFS/ME Service	Guideline	013	009 - 010	We suggest the addition of a review date, and details of how the review will be done.	Thank you for your comment. The Review in primary care section recommends at least once yearly reviews and gives further detail on the review. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. These points are made in the guideline and for this reason your suggestion has not been added to the recommendation
North Bristol NHS Trust - CFS/ME Service	Guideline	013	006	We suggest that this sentence includes the word goals as well as hopes, plans and priorities.	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to delete these bullet points.
North Bristol NHS Trust - CFS/ME Service	Guideline	014	027	We suggest an addition: "and there are a number of ways in which they can be supported with this adjustment that can include psychological support."	Thank you for your comment. This recommendation is to give an overview of ME/CFS and there is more detail throughout the guideline on aspects of ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later in the care and support section of the guideline and for this reason your suggestion has not been added to the recommendation.

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North Bristol NHS Trust - CFS/ME Service	Guideline	021	003 - 010	Overall, this is negative and harsh, and it lacks detail and understanding of current employment practices to the point that we are concerned that it is potentially harmful.	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support.
North Bristol NHS Trust - CFS/ME Service	Guideline	021	004	This is not an appropriate place to start as it is very negative and does not offer a constructive way forward. We suggest an alternative focus such as: Employment and education are important and significant activities in everyone's life and how the person addresses them needs to be central to their management plan. Ascertain their current situation- attendance past and current; their relationship with their manager; length of time in the organisation etc. How they feel about their work; physical, cognitive and emotional challenges including journey to work and activities that facilitate work (meals, laundry, child and pet care) as well as their actual work. Link with self-management strategies including sleep/rest routine, baseline of activity, emotional management etc what can be changed privately first. Provide information about options for support (including reasonable adjustments under the Equality Act and Access to Work assessments) and Then consider what may help within the workplace that can be negotiated either as a reasonable adjustment or flexible working policies. In some cases it may be that the person needs to reduce hours and role significantly or completely leave a job. In that case, the health professionals can provide practical and emotional support and signpost to relevant benefits, careers and employment advice agencies.	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. *Equality Act 2010* In this recommendation there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.
North Bristol NHS Trust - CFS/ME Service	Guideline	021	011	Liaising on the persons behalf may not be possible or appropriate and if done, should not be done without supporting the person firstly self-advocate (perhaps using reports and documents written with the health professional). In addition, it is possible to use resources within the workplace including	Thank you for your comment. The committee agree that the issue of choice and personalised care is fundamental. Liaising with the employers, education providers and support services is in collaboration with the person

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				Occupational health, unions, wellbeing services etc. and resources outside the workplace such as Access to Work and arbitration. The health professional can provide further information and support as required by the person with ME/CFS.	with ME/CFS should only be done when appropriate and in the way that is best for the person.
North Bristol NHS Trust - CFS/ME Service	Guideline	024	General	Energy Management This seems to be using the Adaptive pacing Therapy approach from PACE which was a non-goal directed, symptom contingent approach. It does not look in detail at patterns and habits (possibly long standing) that make this approach difficult to implement and hard to sustain. The psychological impact is not mentioned, and should be clearly stated.	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (See Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and the assessment includes the impact on

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					symptoms/ The energy management plan is part of the care and support plan.
North Bristol NHS Trust - CFS/ME Service	Guideline	025		The approach should consider how to support the emotional frustration and challenge of making these adaptations. Group work and person centred psychological approaches such as CBT, Mindfulness based approaches, compassion focussed therapy and ACT can support people to make significant changes in the way that they adapt to and self-manage manage their health.	Thank you for your comment. No evidence was identified that evaluated incorporating mindfulness with self-management strategies (evidence review G) and the committee have focused on the principles of energy management in this section. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and includes assessment of symptoms on the impact of symptoms on psychological, emotional and social wellbeing.
Optimum Health Clinic Ltd	Guideline	014	019	We would be genuinely interested to the see the figures used to formulate this conclusion and the conclusive statement made in line 22 on the same page. It would be helpful to reference this data at this point in the guidance.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
Optimum Health Clinic Ltd	Guideline	024	004	'..there is no current..cure..for ME/CFS' The rationale behind this statement reflects the limited evidence for any one intervention singularly being effective – such is the nature of the current weight of existing research. We also understand that the guidelines seek to protect vulnerable patients against unscrupulous and unnecessary financial cost or 'promise' of cure, which we wholeheartedly support.	*Thank you for your comment.* *Cure or treatment* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				However, we feel that this statement fails to consider the psychological positioning of a patient reading this document whilst they are in the acute 'crash' phase of this condition. This statement could lead patients to believe that any level of recovery from the 'acute crash phase' is impossible – at worst it implies a definitive 100% recovery failure within this patient group. Any such overt inability to secure positive health improvements is not reflected in the outcomes that we see in clinical practice in reality – where health improvements are certainly achievable. The semantics around 'cure' and 'health improvement' therefore should be elucidated within this messaging we feel. We refer again to the research recently featured at the Institute of Functional Medicine annual conference – which showcased the highly positive clinical outcomes illustrated in a ME/CFS quantitative study which is due for release next year. The link to that presentation is here: https://ifm2020-ifm.ipostersessions.com/default.aspx?s=21-47-90-F6-AC-35-8F-F7-ED-9D-A0-3A-58-55-C9-A3. This study reflects very positive foundational findings, along with highlighting the urgent need for further research into the benefits of integrative and personalised health programmes in the field of ME/CFS. We feel that it would be beneficial if this promising work and the need for further study be referenced in the guidelines. We feel that, when taken in isolation and as a 'soundbite' reflective of the NICE guidance, the 'no cure' messaging could result in despondency and misinterpretation amongst patients. It might also serve to exacerbate the 'maladaptive stress response' that we find to be such a central focus in achieving positive health outcomes within this patient group.	

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				The NICE report itself goes on to describe the possible achievable benefits of working within a multi-disciplinary approach whilst remaining within the 'energy envelope' – therefore we feel that the statement made in 1.11.1 needs further qualification via an extended sentence which should reflect that positive health 'improvements' are indeed possible.	
Optimum Health Clinic Ltd	Guideline	031	006	The recommendation is not to offer ME/CFS patients supplements. This messaging may be slightly confusing to patients, where it is followed by a recommendation to take a multivitamin and mineral in line 18 and vitamin D supplementation in addition. Of course, as an organisation, we have found the individualised use of supplements to be most helpful in supporting the health of ME/CFS clients. A literature review by Werbach in 2000 (https://pubmed.ncbi.nlm.nih.gov/10767667/) draws attention to the suggestion that a number of marginal nutrient deficiencies exist within patients with ME/CFS and these deficiencies may in fact have etiological relevance. This suggests that there may be health supportive benefits associated with correcting these nutrient deficiencies. We find that the nuance between 'treat' and 'support' with reference to nutritional approaches may be key here. But this literature review may provide further support for annual testing of key nutrient markers within this patient group.	Thank you for your comment. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis. The recommendation referring to vitamin D is to manage vitamin D deficiency and not to offer it as a cure for ME/CFS. Recommendation XX recognises it is the person's choice to take vitamins or supplements but that this should be an informed choice with an awareness about potential side effects.
Optimum Health Clinic Ltd	Guideline	032		Regarding referrals for nutrition support: Further to a joint report published by the Royal Society for Public Health and the Professional Standards Authority -which recognises CNHC registered practitioners provide key public health support, and also advocates that Doctors can refer patients to CNHC registrants - we feel that it would be beneficial if the guidance supported referrals to CNHC registered	Thank for your comment NICE's role is to improve outcomes for people using the NHS and other public health and social care services and the recommendations refer to health and social care professionals that are employed within services in the NHS.

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				Nutritional Therapy practitioners with a specific and demonstrable specialism in ME/CFS. NICE estimates that the prevalence of ME/CFS within the UK population sitting at around 260,000. The magnitude of these figures should be considered in combination with the findings of the 2020Health report 'Counting the Cost' published in 2017 - which demonstrated an estimated cost to the UK economy of £3.3 billion in the year 2014/2015 and an estimated £14 billion UK NHS spend dedicated to specialised CFS/ME services. Given the prevalence of ME/CFS in the UK, the current burdens on the NHS and associated Dietetics Services, and the overall cost of these ME/CFS specific services to both the NHS and the UK economy - we feel that CNHC Registered Nutritional Therapy practitioners, who can demonstrate a specialist service provision and/or training in ME/CFS, have much experience to offer to this particular patient group. Therefore, we would request that ME/CFS referrals for dietary and nutrition support should extend beyond NHS based dietetics to CNHC Registered Nutritional Therapists with demonstrable ME/CFS specialisms. Furthermore, we feel that it may be beneficial to see more detailed reference to the extended benefits of dietary and nutrition support for ME/CFS patients (beyond weight management) and feel that perhaps this could be explored further within the guidance.	
Optimum Health Clinic Ltd	Guideline	032	003	Whilst there is a complete lack of evidence to support the use of a single standardised dietary approach or single supplement to 'cure' ME/CFS – and of course the Guidance should serve to protect against this notion - it seems that the specific functional roles that personalised nutrition has to play in offering health 'support' to these patients may not be fully elucidated within the current draft guidance.	Thank you for your comment and information. The committee agree that care for people with ME/CFS should take a person centered approach and recommend this throughout the guideline. In the assessment and care planning section the committee recommend that people with ME/CFS should have a personalised care and support plan, part of the assessment for the plan includes dietary assessment.

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				Without more detailed explanation regarding the potential positive benefits of nutrient balance and dietary support – beyond weight maintenance - we are concerned that the potential benefits of personalised nutrition approaches will be overlooked by the guidance. We refer to the research recently featured at the Institute of Functional Medicine annual conference – which showcased the highly positive clinical outcomes associated with the use of personalised nutrition approaches in ME/CFS. The featured ME/CFS quantitative study is due for release next year. The link to that presentation is here for your consideration: https://ifm2020-ifm.ipostersessions.com/default.aspx?s=21-47-90-F6-AC-35-8F-F7-ED-9D-A0-3A-58-55-C9-A3.	
Optimum Health Clinic Ltd	Guideline	032	011	We wholeheartedly concur with the therapeutic consideration of vitamin D for ME/CFS patients – given their tendency towards a housebound lifestyle. Additionally, research forges links between vitamin D sufficiency and vascular/endothelial health, oxidative stress and inflammation, chronic pain and immune function – all if which are of particular interest in the context of the ME/CFS patient group. However, we should be mindful that there is a safe upper limit to be considered relative to vitamin D supplementation -therefore we would recommend that annual testing of this marker be completed in the proposed yearly review of the care and management plan. Patients reading this current draft guidance would not be aware of such safety concerns around vitamin D supplementation otherwise. In fact, we would be delighted to see a more comprehensive schedule of bloodwork completed annually within the context of the proposed annual care review - which might consider other potential markers for fatigue such as iron status and thyroid function for example.	Thank for your comment. The recommendation includes the link to the NICE guideline on vitamin D for advice on vitamin D supplementation. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The importance of using clinical judgment when deciding on additional investigations is emphasised.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	The CMRC PAG generally welcomes the new guideline. In particular, we welcome the removal of GET and CBT as so-called treatments for this illness, and, just as importantly, the rejection of the flawed rationale behind these interventions. In the absence of treatments or a cure, the primary aim of the guidelines should be to reduce disease burden and suffering, with a view to rehabilitation where appropriate and recovery when it might be possible. In this respect, the draft guidelines are a vast improvement on the previous implementation. We welcome the patient-centred approach of the new guidelines, but we feel there is a lack of clarity about how certain recommendations are to be implemented.	Thank you for your comment. The NICE implementation team are assessing the resource impact of recommendations. We acknowledge that there is likely to be an increase in specialist resources required in some parts of the country in order to make the provision of care more equitable than it has been in the past. Commissioners will decide how best to implement this locally. We note that the recommendations do not emphasise continued involvement by the specialist team. Instead, the focus is on an initial assessment and management plan by the team. Follow up should continue to take place by the general primary care team.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	The guideline revision takes quite a lot of stuff away but doesn't bring anything new to the table. Patients are left with self-management, largely consisting of activity (energy) management. This is much better than patients being given bad or potentially harmful advice, but it is also a stark reminder of the lack of progress in understanding and treating this illness. Therefore, treatments to manage symptoms should be fully explored with patients, and clinicians should be receptive to suggestions from patients regarding possible pharmacological and non-pharmacological interventions that may help on an individual basis.	Thank you for your comment. After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT.

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					When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	The draft guideline is lacking in detail about how specialist ME/CFS clinics and services should look in the future, and places too much emphasis on the role of already-overburdened GPs. The NHS provision for ME/CFS services needs radical overhaul. The current system is a mismatch of different services implementing different approaches. Specialist care for ME/CFS patients is currently a postcode lottery. In addition, services are particularly sparse outside of England, a fact this is not acknowledged in the draft guideline. To implement the recommendations in the draft guideline there are going to have to be substantial and timely changes. The services need a level of standardization so that patients know roughly what to expect when they engage with the services. Each specialist clinic should be staffed by an interdisciplinary team led by a clinician who has a firm up-to-date understanding of ME/CFS, but the makeup of such 'specialist teams' is not specified in the draft guideline. We have concerns that without significant further funding of such services, the new recommendations will not be implemented, and the historical issues will remain.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS

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					the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	Activity (or energy) management advice and the concept of an energy envelope are too simplistic, and its utility is overstated. It is not immediately clear how 'energy management' is different from pacing, a strategy (and terminology) that is familiar to patients. 'Symptom-contingent pacing' is perhaps better terminology. Unlike the energy envelope analogy, symptom-contingent pacing allows for the quite drastic swings in symptom severity that do not seem to fully correlate with activity level or exertion.	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the commissioned report on children and young people) and their own experience. This section of the guideline provides information on the principles of energy management and is clear that it includes all

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					types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	The application of CBT for ME/CFS recommended in this guideline is inconsistent with the theoretical model and assumptions on which it is based. The type of CBT historically applied to ME/CFS relied on a theoretical model that "supposes that unhelpful interpretations of symptoms, fearful beliefs about engaging in activity, and excessive focus on symptoms are central in driving disability and symptom severity. These cognitive responses are associated with unhelpful behavioural patterns, including avoidance of activity or all-or-nothing behaviour—a pattern of excessive resting alternating with pushing too hard or being overactive when well." [Chalder T, Goldsmith KA, White PD, Sharpe M, Pickles AR. Rehabilitative therapies for chronic fatigue syndrome: a secondary mediation analysis of the PACE trial. Lancet Psychiatry. 2015 Feb;2(2):141-52. doi: 10.1016/S2215-0366(14)00069-8. Epub 2015 Jan 28.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. There was concern, particularly from the lay members of the committee, about the wording of CBT manuals that make

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				PMID: 26359750.] This framework is not consistent with the recommendation of CBT for ME/CFS patients in these guidelines [P34, L16–18], which states that CBT for ME/CFS "does not assume people have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS". In addition, the CBT model also invokes the so-called deconditioning hypothesis, which has been rightly rejected in the current draft guidelines. With the rejection of the model(s) underpinning CBT for ME/CFS, the utility of CBT for ME/CFS becomes even more questionable. We suggest that other standard psychological interventions, such as counselling, should be offered when requested by the patient to help them come to terms with their illness and changes in circumstances.	suppositions about 'wrong' cognitions. The committee considered that the narrative around fear avoidance and false illness beliefs can deny patient experience, as fears can be completely rational and protective against harm. Therefore, the committee decided to specify in the recommendations that CBT does not assume people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of ME/CFS, but recognises thoughts, feelings, behaviours and physiology and how they interact with each other.(See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	Families and carers There is frequent mention of families and carers in the draft guideline. It must be recognised that there are many patients with ME/CFS who do not have/no longer have the support of families and carers despite having the need for them. This should be taken into account throughout the guideline.	Thank you for your comment. The committee acknowledge there are people with ME/CFS that are not fortunate to have additional support from families and carers. Throughout the guideline the committee reinforce the importance of people with ME/CFS receiving the support outlined in their care and support plan.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	General	General	There is nothing in the draft guideline about managing pregnancy, childbirth and after care for women with ME/CFS. Pregnancy, childbirth and after care all require a great deal of thought and planning. In addition, pregnancy can be a time of significant change in symptom severity in some patients. Patients have found that the specialist ME/CFS clinics could give no such advice as there was no evidence due to the lack of any research.	Thank you for your comment. The committee agree this is an important area with very little information available for clinicians and pregnant women with ME/CFS. As you note the evidence in this area is sparse and none was identified to support the committee in developing any recommendations.

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				Even if there is no evidence-based recommendations can be given in the current guideline regarding women facing pregnancy and birth, or making decisions about pregnancy, this is an area that should be flagged as needing research.	The committee hope that the focus in the guideline on personalised care and regular review of care would prompt the necessary planning required for pregnant women through to and including the post-natal period. To raise awareness of this gap in the evidence pregnant women and women in the post-natal period have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	004	013 - 015	'is a fluctuating condition.... ranging from being able to carry out most daily activities to severe debilitation'. As it is written, this point fails to convey that each person with ME/CFS will have a range of fluctuation in their "baseline" of symptoms, and that this range itself will change over time.	Thank you for your comment. The aim of the recommendation is to raise awareness that ME/CFS is a fluctuating condition in which a person's symptoms can change unpredictably and sometimes quickly. Further information on the range of fluctuations would not help to clarify the recommendation.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	004	010 - 011	'in its most severe form it can lead to substantial incapacity'. One definition of ME/CFS requires that activity level be 50% or less of the activity level prior to becoming ill. We suggest replacement of this text with 'even in its milder forms it involves substantial incapacity'.	The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity andhave difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. *Definitions of severity* The committee agreed that the impact of severity exists along a continuum and is not easily categorised. However, to provide an overview of the spectrum of ME/CFS definitions of severity have been included in the guideline to provide some context.
Patient Advisory Group to the	Guideline	004	007	Replace 'can have' with 'has'.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are

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CFS/ME Research Collaborative					people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	005	019 - 026	Acknowledgement here is welcome.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	005	012	'regular monitoring and review' is welcome. ME/CFS can lead to a wide range of symptoms but even new or worsening of symptoms fitting an ME/CFS profile should be investigated to check they are not masking a new problem or diagnosis.	Thank you for your comment. The committee agree and the importance of investigating new or worsening symptoms is recommended in the review section of the guideline.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	006	008 - 027	As currently written, this section implies that patients who are not severely (or very severely) affected would not be expected to present with the symptoms in this list. This is not the case. The distinction is that in severe and very severe cases the level of severity of these symptoms is increased. We suggest appropriate revision of this text.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section.

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					To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	006	020 - 021	Add 'insomnia'.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	006	022 - 023	Add 'gastroparesis'.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	006	026 - 027	Include 'orthostatic intolerance and autonomic dysfunction' not just 'postural orthostatic tachycardia syndrome (POTS) and postural hypotension'.	Thank you for your comment. Orthostatic intolerance and autonomic dysfunction have been added to clarify postural orthostatic tachycardia syndrome (POTS) and postural hypotension are examples of orthostatic intolerance.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	006	007	General comment for section 'Awareness of severe or very severe ME/CFS and its impact' The features and implications described here could in most instances also apply to mild and moderate patients. It is the degree of severity of symptoms, the frequency and duration of the symptoms and degree of resulting disability that varies between patients of different severities.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those

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					symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	008	009	Can the core baseline investigations be specified with acknowledgment that the list is not comprehensive? If orthostatic intolerance is present should this be investigated by measuring lying and standing heart rate and blood pressure using the 10-minute active stand test to identify POTS (as a treatable feature of ME/CFS)? The title table test is also widely used to diagnose POTS. Patients with orthostatic intolerance but a negative tilt table test can still benefit from treatments to help manage their symptoms.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	008	016	'symptoms are new and had a specific onset'. It is generally accepted that the specific onset is in most cases an infection, and in some cases the combination of an infection and stress. We suggest appropriate revision of this sentence to reflect this fact.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. To note the committee doesn't assume the triggering event is an infective episode. The first recommendation in the guideline is, Be aware that ME/CFS is a ……… its pathophysiology remains under investigation'. In addition this text is in the context section, 'It is not clear what causes ME/CFS and the pathophysiology of ME/CFS remains under investigation. In many cases, symptoms are thought to have been triggered by an infection but it is not

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					simple post-illness fatigue. It lasts longer and even minimal mental or physical activity can make symptoms worse.'
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	008	016	It must be remembered that in some cases onset is gradual and without an obvious trigger.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes the cohort of people who develop symptoms gradually sometimes over months or even years.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	008	017	post-exertional symptom exacerbation after activity that <u>may be</u> delayed in onset by hours or days not 'is' delayed.	Thank you for your comment. The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	009	002 - 016	Include reference to neurological symptoms. These are included in the earlier symptom list for severe and very severe patients, but these are routinely found in moderately-affected patients. We suggest addition of a bullet-point to read 'neurological symptoms, such as blurred or double vision, and other visual dysfunction, as well as tinnitus and hyperacusis'.	Thank you for your comment. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that neurological symptoms should be included in the list of associated symptoms. They noted that in the evidence reviewed visual dysfunction was this was highlighted in 3 of the 9 criteria and tinnitus and hyperacusis not mentioned at all.
Patient Advisory Group to the CFS/ME	Guideline	009	004 - 006	Orthostatic intolerance also manifests as a feeling of extreme unwellness on sitting or standing, cognitive difficulty, urgent need to sit/put feet up/lie down. If orthostatic intolerance is present should this be investigated by measuring lying and standing heart rate and blood pressure using the 10-minute active stand	Thank you for your comment and information. The committee note there is additional information on orthostatic intolerance in the management of symptoms section of the guideline and in evidence review G.

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Research Collaborative				test to identify POTS (as a treatable feature of ME/CFS)? The tilt table test is also routinely used to diagnose POTS. Patients with orthostatic intolerance but a negative tilt table test can still benefit from treatments to help manage their symptoms.	
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	010	017 - 021	Addition of a bullet point to read 'to avoid any known stressors'.	Thank you for your comment. This recommendation starts with 'give people personalised advice about managing their symptoms' avoid any known stressors would be more specific to the individual and included here. As with all examples in recommendations they are not intended to be exhaustive.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	010	017 - 020	The energy envelope approach and rest as needed is very welcome	Thank you for your comment. After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on pem and energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	010	018	Technical note: 'Energy envelope' link points to wrong definition and needs amending.	Thank you for this comment. To note energy envelope has been deleted in this recommendation.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	011	005 - 006	Who is making the diagnosis? It looks like this text refers to GPs in primary care, but historically many patients have received their diagnosis after being referred to a specialist clinic or a consultant in secondary care. Many GPs simply don't feel comfortable diagnosing ME/CFS, or they may feel they don't have an appropriate knowledge base. Should further referrals and investigations be undertaken to investigate symptoms, these are unlikely to have been completed within this 3-month period. Do patients in these circumstances receive an ME/CFS diagnosis and referral to a specialist team? Or do they wait potentially many months without specialist input until all other potential diagnoses are ruled out?	Thank you for your comment. The qualitative evidence and the committee experience reflect your comments about the lack of confidence in GPs in diagnosing ME/CFS. The committee agreed it was not clear in the recommendations about when a diagnosis is made and after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for a diagnosis for both the clinician 'provisionally diagnosing' and the person with the symptoms. • It has been clarified that if symptoms continue for 3 months then a person should be referred to a ME/CFS specialist team for confirmation of the diagnosis (this is adults is most likely from primary care and in children and young people they referral is from a paediatrician). It is at this point a detailed assessment is then recommended. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The importance of using clinical judgment when deciding on additional investigations is emphasised and as with all clinical decision making it is individual to the circumstances of the patient around the timing of these and appropriate referral.
Patient Advisory Group to the CFS/ME	Guideline	011	007 - 008	NICE should be aware that these specialist services are patchy and could be described as a postcode lottery. Many NHS trusts do not provide a specialist ME/CFS service, and patients are instead channelled to various different consultant-led clinics, such as rheumatology. It is not clear in the draft guidelines what	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people

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Research Collaborative				should happen in these instances. Should patients be referred to the nearest specialist ME/CFS clinics?	are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. The committee note that throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. *Service design* This guideline focused on clinical care and service delivery was not included as part of the scope of the guideline and the committee are unable to make recommendations on the specific design of services. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment to allow access to services. This guideline highlights areas where the specialist team should focus on (e.g. assessment. and development of a care plan) and those areas that should be done in primary care (e.g. initial diagnosis and review).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	011	013	General 1.5 Assessment and care planning by a specialist ME/CFS team There is no clarity in the guideline about which specialisms will be represented in an ME/CFS specialist team. A rough template for these teams should be specified. Will patients be initially	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the

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				assessed by a medically qualified doctor? This is particularly important when considering pharmaceutical treatment of symptoms. Currently, patients often have no contact with a medically qualified doctor when they are referred to specialist ME/CFS services.	management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	012	017 - 018	The inclusion of mobility aids and adaptations in the management plan to increase or maintain independence is welcome.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	013	009 - 010	We welcome this suggestion.	Thank you for your comment.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	013	012 - 013	Home visits for severe and very severe ME/CFS patients are welcome. Did NICE consider the option of remote appointments for moderately-ill patients, or patients who live some distance away from the nearest clinic? The length of travel and appointment time must be considered as this can have a detrimental effect on even mildly unwell patients.	Thank you for your comment. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the assessment and development of the care and support plan but other methods may be more appropriate depending on the person's symptoms.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	013	006	It is fine to record plans and priorities but care should be taken with 'hopes' to ensure that patients are not misled as to long-term outcomes or encouraged to 'have motivations to help them recover' which is a common current narrative from healthcare workers.	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to delete these bullet points.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	009 - 014	We suggest that supplying information suitable for sharing with schools, universities, workplaces, the DWP, etc., would be both appropriate and beneficial to patients.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	001 - 003	Suggest addition of 'how their ME/CFS affects them and their ability to access information'.	Thank you for your comment. Symptoms has been added here to reflect the impact of their ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	022 - 024	Acknowledging the small percentage of patients who fully recover is welcome. This enables realistic planning for the future. Add 'long-term' to the end of this sentence.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	025 - 027	Change to '<u>will</u> need to adjust how they live'.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	006	The use of music activities to communicate with children with ME/CFS seems an odd recommendation given the noise sensitivities experienced by many patients. Is there robust evidence behind this recommendation?	Thank you for your comment. These are examples of formats supported by the committee's experience. They considered that some children and young people with ME/CFS may find this helpful.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	014	019	Are periods of remission and relapse common? Would this be better described as fluctuations?	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet points and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	015	001 - 003	Honesty here is important and welcome. Not all children will recover.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	015	023	The diagnosis of ME/CFS in a child, parent, partner or other family member is serious and can be devastating. What consideration has been given to the emotional support needs of parents, children, partners and family members of those diagnosed? There is currently no provision for diagnosis-specific support. Is it possible to learn from the support given to parents of children diagnosed with other long-term, life-changing illnesses, and was this considered by NICE?	Thank you for your comment. The committee agree that supporting families of people with ME/CFS is important and have made recommendations for them throughout the guideline where the evidence and their experience supported this.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	015	023	The clarity of this section is welcome, in particular acknowledgement of the risk of symptoms being confused with signs of abuse and neglect [P16, L10–11] and the recognition of what is not necessarily a sign of abuse or neglect [P17, L8–19]	Thank you for your comment.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	016	006	Section 1.7.1 reads as if safeguarding should automatically be carried out which we feel is not what is intended. We suggest addition of 'Where necessary' at the start of this line.	Thank you for your comment. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	017	020	Recognition of the difficulties and barriers to accessing care is welcome	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	018	019 - 024	Moderately affected patients and some mildly affected patients also need some of these provisions. Patients who manage to access appointments and may not appear badly affected at the time suffer post-exertional symptom exacerbation as a result.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	018	015	Replace the word 'fear' with 'risk'.	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
Patient Advisory Group to the CFS/ME	Guideline	018	018	Suggest addition of a third bullet point that reads 'patients may pace their activity and rest more in the days before an appointment to minimise their symptoms in order to be well enough to attend'.	Thank you for your comment. This recommendation raises awareness about the reasons people may miss an appointment not about preparation for an appointment and for that reason your suggestion has not been added.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	019	004 - 007	Suggest addition of a third bullet point to read 'the availability of food and drink for patients with dietary requirements and food sensitivities and any meal timing requirements (for example, shifting meal times due to symptoms such as nausea).'	Thank you for your comment. The recommendation includes to discuss the person's care and support plan and gives examples of what could be discussed. Dietary considerations would be included in the care and support plan and the examples given are not meant to be exhaustive. For this reason your suggestion has not been added.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	019	008	Moderately affected patients and some mildly affected patients may also require some of these provisions	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or hospital can be difficult. This section does make a recommendation for all people with ME/CFS and includes that any difficulties in accessing hospital care should be discussed and gives some examples of what should be considered. These are expanded on for people with severe or very severe ME/CFS taking into account there are further challenges to consider.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	019	011	A clear plan is needed for requirements when staying in hospital and ensuring that the plan and the importance of the requirements are shared with the ward staff.	Thank you for your comment. The recommendation includes discussing the person's care and support plan to plan any adjustments, the aim would be to communicate this information to the hospital and the ward staff.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	020	020 - 030	These recommendations are welcome. Specialist clinics should be able to provide aids or prescriptions for aids.	Thank you for your comment.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	020	028	Some adaptations are mentioned but it may be useful to mention others, for example bath lifts, stair rails, and perching stools.	Thank you for your comment **These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.**
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	021	014	and/or provide the patient with information for the patient to share.	Thank you for your comment. The information and support section of the guideline has recommendations on providing information and this applies throughout the guideline. For this reason this suggestion has not been added.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	022	010 - 012	Very welcome advice that children and young people with ME/CFS need a balance of activities in their life, and that schoolwork should not be the only activity they undertake.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	022	005	Include recommending exam access arrangements. In addition to mentioning online education it would be good to add 'consider funding online education'. Home education should be scheduled to avoid times of the day when a child or young person is likely to be at their worst.	Thank you for your comments. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	022	07	Suggest addition of 'and provide information about support available to help with the application e.g., SENDIASS.'	Thank you for your comment. This is a broad recommendation about providing advice, the detail of the advice and support needed will depend on the child or the young person. For this reason your suggestion has not been added.
Patient Advisory Group to the CFS/ME	Guideline	022	013	General comment for the Multidisciplinary Care section We suggest the addition of 'Care for patients should be ongoing with regular reviews. Patients must not be discharged and left	Thank you for your comment. The review section of the guideline covers review of care and the discussion section of the review.

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Research Collaborative				without specialist support when living with this debilitating long-term condition.'	Discharge The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. For these reasons your suggestion was not added to the recommendations.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	024	006 - 024	Patients generally refer to this approach as pacing. Periods of rest must be included. A reduction in the intensity of activity is generally necessary, not just a reduction in the duration. Patients should be encouraged to listen to their bodies and never ignore signs that they need to stop.	Thank you for your comment. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Patient Advisory Group to the CFS/ME	Guideline	024	004 - 005	Acknowledgement that there is no current treatment or a cure is welcome.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is

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Research Collaborative					alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	024	019	With children and young people it can be helpful to explain the principles of pacing and energy management to parents so that they can help spot patterns, provide advice and manage their expectations (i.e., be patient when a child/young person cannot do something).	Thank you for your comment. Throughout the guideline the committee have emphasised the importance of including the parents or carers of children and young people with ME/CFS where appropriate and this section is no exception.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	025	001 - 002	It must be acknowledged that some patients may not improve and won't be able to increase tolerance or activity. Some patients may deteriorate over time. This is not their fault and they must not be blamed. This is the nature of the condition. It should not be assumed that they are doing anything wrong in their management approach. If a patient's health improves they may naturally and instinctively be able to gradually do more.	Thank you for your comment. After considering the stakeholder comments recommendation 1.11.6 this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).' In the section of flare ups and relapses the committee have added a recommendation raising awareness that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	025	003	Assertion that energy management 'does not assume that deconditioning is the cause of ME/CFS' is welcome.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	025	005	Acknowledge that a patient's desired goals (which for most will be full recovery and the resumption of their pre-illness level of activity) may be unrealistic, at least in the short term and for many in the long term. Support patients to cope with this realisation and its implications.	Thank you for your comment. The committee discussed the use of goals and agreed that where they were included it was important that people should be supported to establish realistic expectations and develop goals that are meaningful to them. This is in line with the holistic personalised approach the guideline adopts and will include discussion about where goals are unrealistic. The committee acknowledge that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed and the committee have added a recommendation raising awareness about this in the flare up and relapse section of the guideline.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	025	018	Change to 'Reduce the intensity and duration of activity as the first step'.	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	026	004 - 005	How is it to be assessed if a patient is 'ready to progress their physical activity'? Perhaps the referral should be if patients 'want to explore the possibility and suitability of progressing their physical activity'. Progressing physical activity may not be possible to do safely, even with specialist input. GET does not become safe just because a patient is willing to do more.	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. Then as you say the referral is to explore this possibility.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	026	006 - 007	It must be clear that this is not GET. GET is not safe. If this is not a recommendation of GET, how does it differ? This should be made much clearer.	Thank you for your comment. The principles of the energy management plan include that it is about all types of activity and uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). This is different to graded exercise therapy. In addition the next section of the guideline includes do not offer, 'any programme that does not follow the approach in recommendation 1.11.15 or uses based on fixed incremental

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					increases in physical activity or exercise, for example graded exercise therapy.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	026	014 - 015	Change to '...that increases in activity should be smaller and much slower.' There is no reason why decreases in activity should be small—they may need to be significant. There should be no assumption that a patient will be improving and hence able to increase their activity.	Thank you for your comment. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee included (if possible) to emphasise that any increases may not be possible and are not assumed.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	026	003	'long time' in this sentence is vague and subjective. Please consider clarifying.	Thank you for your comment. 'for a long time' has been removed and a link to has been added to this section.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	027	021 - 023	We strongly welcome these recommendations.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	028	001 - 011	We strongly welcome these recommendations.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	028	012 - 015	How is it to be assessed if a patient is 'ready to progress their physical activity'? Progressing physical activity may not be possible to do safely, even with specialist input. Increasing physical activity does not become safe just because patients want to do more. The phrase 'ready to progress' implies improvement is to be expected. Could it be rephrased as ''who are experiencing an improvement or remission'?	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. Based on the quantitative and qualitative evidence (evidence reviews A, F,G and H) and their own experience the committee concluded that it was important that a physical activity or

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					exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	028	019 - 022	A mechanism for reporting adverse outcomes from supervised physical activity programmes is necessary. It should be made clear that worsening of symptoms after physical activity programmes can be long term; GET has made a significant proportion of patients permanently more unwell and disabled. Patients must be informed of this so that they can give informed consent to any physical activity program.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	029	006 - 016	Consider whether a physical activity program is appropriate at all if a patient suffers a flare or deterioration of symptoms as a result of undertaking a physical activity program. A system through which patients can report any harm is necessary.	Thank you for your comment. This is a personalised physical activity or exercise programme that is initially explored with the person with ME/CFS and then if appropriate to undertake overseen by a ME/CFS specialist physiotherapist and reviewed regularly.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	029	006 - 016	Mental, physical and emotional activity all use up a person with ME/CFS's energy, and any physical activity should be considered alongside other energy usage to ensure balance both as a program and on a day-to-day basis. In addition, any activity plans should take account of changes in sleep patterns.	Thank you for your comment. The committee agree that all of the person's activities should be considered when developing an energy management and if appropriate a physical activity plan.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	029	017	Comment on Rest and Sleep section Many patients find that they need to sleep more frequently and for longer than before they became ill and that attempts to restrict sleep often make them more unwell. Patients should not be recommended to restrict sleep, nor should they be told to fight sleep reversal. Failing to mention sleep management in these guidelines leaves open the risk that sleep restriction could still be recommended to patients to detrimental effect.	After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	030	013 - 016	This section is particularly sparse. A brief summary of the wide prevalence of pain—and its different forms—should be included here. Even in the absence of evidence to recommend any particular intervention the reality of pain in ME/CFS should be acknowledged. Are there no other relevant guidelines other than the two linked in this section, for example inflammatory pain?	Thank you for your comment. The committee agree that people with ME/CFS report many different types of pain. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	030	003	We suggest that patients should be referred for investigation and treatment for autonomic dysfunction and orthostatic intolerance if they report such symptoms, not simply if their symptoms are 'severe or worsening'. If orthostatic intolerance is present this should be investigated by measuring lying and standing heart rate and blood pressure using the 10-minute active stand test to identify POTS (a treatable feature of ME/CFS). The tilt table test is also widely used to diagnose POTS. Some patients with orthostatic intolerance will have a negative tilt table test but still need treatment to help manage their symptoms.	Thank you for your comment. In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	031	001	This advice on managing nausea seems limited. Patients may benefit from anti-sickness medicines. Did NICE consider this?	Thank you for your comment. The evidence for any pharmacological interventions for ME/CFS was inconclusive with limited evidence for any one medicine and this was supported by the committee's clinical experience and consensus view. As a result the committee could not confidently recommend any medicines. To note the recommendation on nausea has been moved to the section on dietary management and strategies.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	032	001	Many people with ME/CFS have symptoms of IBS and food intolerances. This is not addressed in the guideline. These patients may need the support of a dietician and may benefit from a particular diet, e.g., the low FODMAP diet. We suggest linking to the Nice Guideline for Irritable Bowel Syndrome.	Thank you for your comment. The NICE Guideline for Irritable Bowel Syndrome has been added to the list of NICE guidance in the coexisting conditions section of the guideline.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	032	018	Is it worth mentioning that a multivitamin may be recommended due to a poor quality diet (for example, as a result of nausea or lack of appetite making it hard to eat a balanced diet).	Thank you for your comment. The evidence did not allow conclusions to support people routinely taking vitamins or supplements either as a cure for ME/CFS or for managing symptoms and a recommendation was made to reflect this.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	033	014	There is a reference to nutrition guidelines for adults but children can also have severe ME/CFS and consequential nutritional problems. This needs to be acknowledged and appropriate advice given or advice to refer to a specialist.	Thank you for your comment. This recommendation links to the NICE guideline on nutritional support for adults, there isn't a similar NICE guideline for children. This recommendation doesn't assume children or young people do not need nutritional support. There is recommendation to refer children and young people with ME/CFS who are losing weight or have faltering growth or dietary restrictions to a paediatric dietitian who specialises in ME/CFS. In addition the initial recommendation in this section, ' refer people with severe or very severe ME/CFS for a dietetic assessment by a dietitian who specialises in ME/CFS' includes children and young people.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	034	014 - 018	CBT is not a treatment nor a cure for ME/CFS yet it is still being recommended with the aim to 'improve functioning' and 'recognising that thoughts, feelings, behaviours and physiology interact with each other'? These statements are concerning given the history of using CBT as a supposed treatment/cure for ME/CFS.	Thank you for your comments. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	034	001	Psychological support for the psychological and practical impacts of an ME/CFS diagnosis is welcome but why is CBT in particular the (only) therapy recommended? Would counselling by a practitioner with understanding and experience of ME/CFS, for example, not be (potentially more) helpful? CBT as specifically applied to ME/CFS has historically been based on a now discredited illness model—namely that any lack of progress and persistence of illness was in large part due to patient's beliefs and fears about their symptoms and functioning. As such, the CBT model for ME/CFS is not appropriate.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	034	001	CBT seems much less appropriate than counselling for people with ME/CFS, given the enormous losses (employment, independence, relationships, choices, etc) suffered by people with ME. Psychological support should offer help with the grief caused by this illness, and only if possible should psychological support attempt to aid symptom management.	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	034	026	Working towards 'meaningful goals' in ME/CFS? If these goals are to increase function then CBT cannot offer this; it is not a treatment nor a cure.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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					CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	034	017 – 018	"... BUT recognises that thoughts, feelings and… physiology all interact with one another." The phrasing here seems to undercut the first part of the sentence. It needs to be clear cut that 'abnormal' illness beliefs do not underlie ME/CFS. Suggest stopping the sentence after "cause of their ME/CFS" .	Thank you for your comment. There was concern, particularly from the lay members of the committee, about the wording of CBT manuals that make suppositions about 'wrong' cognitions. The committee considered that the narrative around fear avoidance and false illness beliefs can deny patient experience, as fears can be completely rational and protective against harm. Therefore, the committee decided to specify in the recommendations that CBT does not assume people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of ME/CFS, but recognises thoughts, feelings, behaviours and physiology and how they interact with each other.(See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	035	005 - 011	Is this not just good management advice that should be offered already without calling it CBT?	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	035	007	Sleep restriction (for those needing to sleep more than unusual) and efforts to alter sleep timings (or address sleep reversal) can make things worse not better for some people with ME/CFS	Thank you for your comment and information.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	035	014	It must be clear that children and young people (and adults too of course) can refuse CBT without this impacting on their ongoing care.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At the start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	035	023	Huge care should be given with any counselling for people with severe or very severe ME/CFS. It is worth painting back to paragraphs 1.1.8 to 1.1.10 and particularly 1.1.11 and the need for a risk assessment.	Thank you for your comment. The committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or focusing for periods of time can be difficult, and particularly so for people with severe or very severe ME/CFS. As you note the access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as

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					examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. As you note the recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	036	005 - 006	Did NICE not find enough evidence in the literature to state with confidence the main coexisting conditions—for example, IBS, fibromyalgia, and POTS—that have a high prevalence in ME/CFS patients? A list here might be helpful for GPs who are not as familiar with ME/CFS as the patient may like.	Thank you for your comment. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not

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					infer any importance of the condition in reference to co-existing with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	037	015 - 017	GPs and other healthcare professionals should be open to investigating any other possible reason for a deterioration in health, an increase in symptoms, or new symptoms in patients, and should not assume that they are the result of ME/CFS.	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	038	020 - 021	Why wait until resolution or stabilisation before investigating symptoms? If viable, investigation should take place in a timely manner. Resolution may not happen at all, and stabilisation may take a long time. New symptoms may reflect an additional problem which may require timely treatment.	Thank you for your comment. This section has been reordered and in summary, strategies to manage flare ups and relapses should be included in the care and support plan, if a flare up and relapse cannot be managed then the person should contact their named contact for support, in particular for a relapse (if a review is needed) there are some examples of factors to consider. The committee hopes this adds clarity to this section. The committee agree that some people with ME/CFS may require more regular reviews depending on the severity and complexity of their symptoms.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	039	013 - 018	An accurate medical record of a patient's condition is required as evidence for benefit claims so it is very important that this is regularly recorded in detail.	Thank you for your comment. The recommendations in the review section of the guideline include the minimum areas for assessment and documentation for all people with ME/CFS. This is not intended to be an exhaustive list and should be tailored according to the individual. These areas can be used as the basis for a discussion on accessing disability support where appropriate.

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					The committee noted in Evidence review J: Review of Care that written assessments, and reassessments, are important for accessing disability support and a scheduled review is such an opportunity.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	039	002 - 004	A review once a year is welcome. It is important for patients to know who is in charge of their medical care related to their ME/CFS and to be regularly reviewed. Currently, GPs may assume that the medical care related to the patient's ME/CFS is being managed by the specialist clinic when in reality the patient may never have been seen by a doctor or a nurse in clinic, but rather by a psychologist, physio or OT who are unable to advise on medical matters. Currently, if a patient is not under the care of a specialist clinic the GP may not even register that ME/CFS is an ongoing issue despite it being historically recorded on the notes.	Thank you for your comment. The committee agree and hope these recommendations address this confusion.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	039	001	General Comment on Review section ME/CFS patients can often become lost in the system. Patients can find themselves discharged from specialist clinics with no suggestion of review and no plan, and left in the hands of their GPs who may not be well-versed in current knowledge of ME/CFS. We therefore welcome these recommendations and hope that they are implemented in full.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	039	010	Typo ME/CF should be ME/CFS	Thank you for your comment. This has been corrected.
Patient Advisory Group to the CFS/ME	Guideline	039	015	It should not be assumed that new symptoms or a worsening of symptoms is due to ME/CFS and, where appropriate, other causes should be investigated or ruled out as they would be for non-ME/CFS patients.	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a

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Research Collaborative					change in symptoms are investigated. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This has been reinforced in the flare up and relapse section of the guideline.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	040	011	General Comment for 1.15 Training for health and social care professionals We note that there is a need for further and improved up-to-date training for all DWP and benefit assessors, as well as in medical schools and university settings. NICE should consider a recommendation that the content and material provided is standardized, instead of varying significantly from clinic to clinic, as is the case currently.	Thank you for your comment. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula and in training for all DWP and benefit assessors. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops. See evidence review B for the committee discussion on training.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	040	015	It is important that medical staff including those on hospital wards have training in the issues that ME/CFS patients may have when being admitted for treatment for other issues. This can help ensure that a patient's ME/CFS symptoms are not exacerbated by other treatments.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	040	017	Change to 'provide up-to-date evidence-based content and training methods...'	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. This emphasises the need for up-to-date training programmes. To note the training recommendations have been edited.

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					See evidence review B for the committee discussion on training. This emphasises the need for up-to-date training programmes.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	040	018	There is a potential issue with specialist services developing and supporting training. Given the changes in the draft guideline, a significant change in approach is needed; this will be a challenge for those who have previously been taught and practiced the now discredited GET/CBT style treatment approach. The staff currently running these services may have bias (conscious or otherwise) towards the previous ways of doing things. It is not enough for the guidelines to change—practice must change too. There must be safeguards to ensure this happens.	Thank you for your comment. The final recommendation in this section is clear that training should reflect current knowledge so that health and social care professionals can maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. The development of training by ME/CFS specialist services reflects the evidence in Evidence reviews A and B and the committee's experience that ME/CFS specialist services provide valuable training, information and support to non specialists and people with ME/CFS. See evidence review B for the committee discussion on training.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	041	001 - 004	The importance of up-to-date training and CPD for professionals working in ME/CFS clinics cannot be emphasised enough. A change in approach is needed which will be a challenge for those who have previously been taught and practiced the now discredited GET/CBT style treatment approach. It is not enough for the guidelines to change—practice must change too. Also, there is a need for urgent updates to GP knowledge.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B for the committee discussion on training. This emphasises the need for up-to-date training programmes.
Patient Advisory Group to the CFS/ME	Guideline	042	007	Patients often refer to their energy and symptom management strategies as pacing.	Thank you for your comment. The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it

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Research Collaborative					would add further to the confusion around this term and for this reason have not included it.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	042	025	Flares are often referred to as 'crashes' by people with ME/CFS.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	043	009 - 019	Definitions of severity are not clear cut. Some symptoms may be experienced in a more extreme way than others for different people with ME/CFS. It would be good if this could be acknowledged here. For example a patient may be reasonably mobile but have significant cognitive difficulties, or vice versa. Every person with ME/CFS has their own unique presentation.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	043	021	Orthostatic intolerance may not involve an 'inability to regulate blood pressure'. E.g. PoTS does not involve an inability to regulate blood pressure; it is characterised by tachycardia on standing with no blood pressure changes.	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as lightheadedness, near-fainting or fainting, impaired concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	044	022	'PEM' is a commonly used acronym for post-exertional malaise. Please add this acronym to this sentence	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	045	001 - 010	Definitions of severity are not clear cut. Some symptoms may be experienced in a more extreme way than others for different people with ME/CFS. It would be good if this could be acknowledged here. For example, a patient may be reasonably mobile but have significant cognitive difficulties, or vice versa. Every person with ME/CFS has their own unique presentation.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	045	012	Typo: provides	Thank you for your comment. This has been edited.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	045	022	There are a number of research recommendations made. But fundamental research needs to be carried out to understand the causes and mechanisms behind ME/CFS. One such project is DecodeME which is a GWAS study but other projects are desperately needed—for example, looking at a range of omics techniques.	Thank you for your comment. The research recommendations are developed from the evidence reviews and as evidence looking for causes and mechanisms of ME/CFS was not reviewed the committee were unable to make a research recommendation on this topic.

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Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	048	009 - 013	It is welcome that this has been acknowledged	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	053	021	It is unclear why CBT is listed amongst other essential aspects of managing ME. It may be worthwhile rephrasing in more general terms, such as 'psychological support may be useful as someone comes to terms with the impacts of ME/CFS'.	Thank you for your comment. CBT is included as it is an option for people with ME/CFS to support them in managing their symptoms.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	054	005	Change to 'may lead to better outcomes.'	Thank you for your comment. This has been edited.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	057	022 - 024	It is welcome that this has been acknowledged.	Thank you for your comment.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	059	017	Change to 'should' or 'may' rather than 'will'.	Thank you for your comment. This has been edited to, 'should'.
Patient Advisory Group to the CFS/ME	Guideline	061	016	Surely harm could be caused to those who are mildly or moderately affected too if strategies are inappropriately applied, particularly when/if increases in activity are being attempted?	Thank you for your comment. The committee agree and have recommended that all people with ME/CFS should receive specialist advice. This section

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Research Collaborative					specifically draws attention to people with severe or very severe ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	063	001 - 008	Patients have reported harm from GET when delivered by ME/CFS specialists. How will physical activity and/or exercise programs overseen by physios or OTs with training and expertise in ME/CFS be free from this risk of harm? Provision needs to be in place for patients to report any harms to an independent body.	Thank you for your comment. It is not within the remit of NICE to recommend an independent body to report harms to.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	065	010 - 014	Where does this lack of recommendation leave patients? Without treatment unless their pain is neuropathic or a headache?	Thank you for your comment. *Pharmacological management* Pain relief was included as an intervention in the protocol for pharmacological interventions. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	067	020	Why is CBT the only psychological support that has been considered here? Has the potential need for counselling or other psychological support to cope with the implications of this life changing diagnosis been considered? A regular opportunity to talk through the ongoing and often changing impact of ME/CFS and the emotions associated with this would be welcome to many. It does not appear that this need has been considered by the committee. Support would need to be provided by someone	Thank you for your comment. Other psychological support was considered. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any

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				with understanding of ME/CFS. In addition, psychological support for family members of those diagnosed would be helpful.	recommendations for any of the interventions (see evidence reports G and H).
Patient Advisory Group to the CFS/ME Research Collaborative	Guideline	071	010	The term 'post-viral fatigue syndrome' (PVFS) also gets used.	Thank you for your comment.
Pernicious Anaemia Society	Guideline	General	General	A Survey of members of the Pernicious anaemia Society (Hooper et.al. 2014 -British Journal of Nursing) showed that 44% of patients were originally misdiagnosed (probably due to the flawed assays being used) and 25% of these were originally suspected of having M.E./CFS and 15% were originally diagnosed as having the condition. This led to many developing serious and irreversible nerve damage. We strongly recommend that patients presenting with the symptoms described in the Draft Guideline have their Vitamin B12 status evaluated. However, physicians should be aware of the unreliability and inadequacy of the current assay used to determine the B12 status of patients. The cost implications are enormous – we recently submitted a report to NICE that stated at the cost of GP consultations leading up to a firm diagnosis of B12 Deficiency was at the very least £16 million in England alone. That's without the costs of secondary tests (MRI Scans, Nerve Conduction Tests etc) was taken into account. We are now working with the James Lind Alliance to address the Uncertainties in the Diagnosis of B12 Deficiency and Pernicious Anaemia but in the meantime, we are concerned that this Draft Guideline does not suggest that patients with the symptoms of CF/ME, which are the same as those for B12 Deficiency/Pernicious Anaemia have their B12 status evaluated at an early stage.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. NICE has commissioned a guideline on Pernicious anaemia.

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Pernicious Anaemia Society	Guideline	008 - 009	010	1.2.3 - These symptoms are identical to Vitamin B12 Deficiency that, if not diet related, will probably be caused by Pernicious Anaemia (Autoimmune Metaplastic Atrophic Gastritis). We thoroughly recommend that before any progress is made in diagnosing CFS/ME the patient be assessed for B12 Deficiency. However, physicians should be aware that the current serum B12 Test is now largely discredited (by the British Committee for Standards in Haematology – see their 2014 Guideline on Cobalamin and Folate Disorders), and any evaluation of the patient's B12 Status should involve the Holotranscobalamin Assay along with MMA and Homocysteine. That should give a more accurate picture of the patient's B12 Status. Please be aware that only 4-40% of patients who have low B12 will have any macrocytosis.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. NICE has commissioned a guideline on Pernicious anaemia.
Pernicious Anaemia Society	Guideline	008 - 009	017	Box 1 - Again, these symptoms are identical to Vitamin B12 Deficiency as above.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. NICE has commissioned a guideline on Pernicious anaemia.
Pernicious Anaemia Society	Guideline	009	002	1.2.4 - As Above – almost identical to the symptoms of B12 Deficiency	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. The importance of using clinical judgment when deciding on additional investigations is emphasised. The examples are not intended to be an exhaustive list.

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Pernicious Anaemia Society	Guideline	009	021	1.2.6 - It's important that the B12 Status of patients should be evaluated – but be aware of the current inaccuracy of the serum B12 assay – please see comment 1 above	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. NICE has commissioned a guideline on Pernicious anaemia.
Pernicious Anaemia Society	Guideline	009	021	1.2.6 - Patients should be asked if there is any history of Pernicious Anaemia in their family as the Schilling Test, which is no longer available, was much better than the current assay in identifying Pernicious Anaemia as being the cause of the patient's symptoms and Pernicious Anaemia is hereditary and based on genes. 15% of members of the Pernicious Anaemia Society had a parent with the same disease and another 15% had a Grandfather with the disease.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. NICE has commissioned a guideline on Pernicious anaemia.
Physios for ME	Guideline	General	General	Physios for ME are extremely pleased with the tone and content of the Draft Guideline and would like to thank all those who have taken part in the development for their role in listening to the concerns of the community and for their understanding of the misconceptions faced by people with ME/CFS over many years and for coming to grips with a very difficult problem. In particular we support the recognition that graded exercise therapy is not appropriate for people with ME due to the evidence of adverse physiological responses to exertion, the qualitative evidence of patient reported harm following graded exercise therapy, and that the evidence review by NICE of non-	Thank you for your comment.

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				pharmacological management for ME/CFS found the quality of evidence of the clinical effectiveness of graded exercise therapy ranged from low to very low.	
Physios for ME	Guideline	General	General	We agree with the comments of Forward ME in relation to recognising ME/CFS as a neurological condition: “ME/CFS is a recognised neurological disease classified by WHO ICD10 G93.3. This classification is also recognised by the Department of Health and Social Care. It is also recognised as a disease by all of the US authorities and by many researchers. It would be consistent if the term ‘disease’ is used throughout in place of ‘medical condition’ which appears to diminish the impact of ME/CFS.”	Thank you for your comment. The text ‘Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context. Condition is a commonly used term in NICE guidelines and it’s use does not diminish the impact of ME/CFS (for example, Multiple sclerosis in adults: management https://www.nice.org.uk/guidance/cg186/chapter/Recommendations).
Physios for ME	Guideline	General	General	We were disappointed to see no mention of the physiological effects of exertion in the review. We feel it is essential for health professionals working with people with ME/CFS to have knowledge of the physiological processes that occur during over-exertion. Research has shown that exercise in people with ME leads to abnormal physiological responses including: 1. reduced maximum heart rate 1-3 2. reduced maximum oxygen consumption 3-5 3. reduced cardiac output 1,2,6 4. insufficient blood pressure increase on exertion 4,7 5. decreased capacity to use oxygen 1 6. anaerobic threshold and maximum exercise are reached at much lower oxygen Capacity 3,8 7. exhaustion reached more rapidly and accompanied by relatively reduced intracellular concentrations of ATP 9 8. increased intracellular acidosis in exercising muscles and reduced post-exercise	Thank you for your comment. The guideline includes a definition of post exertional malaise and describes the impact of activity on people with ME/CFS. Exploring the specific physiological effects of exertion was not prioritised by stakeholders during the development of the scope or by the committee when finalising the evidence review questions. As such evidence on the physiological effects of exertion has not been searched for or reviewed and the committee were unable to make any recommendations on this topic.

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				recovery from acidosis 10,11 9. activation and worsening of symptoms which can be immediate or delayed by several Days 12, 13 10. when exercise is repeated the next day, abnormalities are more severe 14 11. decreased cognitive functioning and prolonged reaction time 15 12. prolonged recovery period: usually 24 hours, often 48 but can last days, weeks or cause a relapse 1,14,16 1. De Becker P, Roeykens J, Reynders M, et al. Exercise capacity in chronic fatigue syndrome. Arch Intern Med 2000;160:3270-77. [PMID: 11088089] 2. Inbar O, Dlin R, Rotstein A, Whipp BJ. Physiological responses to incremental exercise in patients with chronic fatigue syndrome. Med Sci Sports Exerc 2001; 33: 1463-70. [PMID: 11528333] 3. Jones DE, Hollingsworth KG, Jakovljevic DG, Fattakhova G, Pairman J, Blamire AM, Trenell MI, Newton JL. Loss of capacity to recover from acidosis on repeat exercise in chronic fatigue syndrome: a case-control study. Eur J Clin Invest 2012; 42: 186-94.. [PMID: 21749371] 4. Farquhar WB, Hunt BE, Taylor JA, Darling SE, Freeman R. Blood volume and its relation to peak O2 consumption and physical activity in patients with chronic fatigue. Am J Physiol Heart Circ Physiol 2002; 282: H66-71. [PMID: 11748048] 5. Jammes Y, Steinberg JG, Mambrini O, Brégeon F, Delliaux S. Chronic fatigue syndrome: assessment of increased oxidative	

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				stress and altered muscle excitability in response to incremental exercise. J Intern Med 2005; 257: 299-310. [PMID: 15715687] 6. Peckerman A, La Manca JJ, Dahl KA, Chemitiganti R, Qureishi B, Natelson BH. Abnormal impedance cardiography predicts symptom severity in chronic fatigue syndrome. Am J Med Sci 2003; 326: 55-60. [PMID: 12920435] 7. Streeten DH. Role of impaired lower-limb venous innervation in the pathogenesis of the chronic fatigue syndrome. Am J Med Sci 2001;321:163-7. 8. Vermeulen RCW, Kurk RM, Visser FC, Sluiter W, Scholte HR. Patients with chronic fatigue syndrome performed worse than controls in a controlled repeated exercise study despite a normal oxidative phosphorylation capacity. J Transl Med 2010; 8: 93. [PMID: 20937116] 9. Wong R, Lopaschuk G, Zhu G, Walker D, Catellier D, Burton D, Teo K, Collins-Nakai R, Montague T. Skeletal muscle metabolism in the chronic fatigue syndrome. In vivo assessment by 31P nuclear magnetic resonance spectroscopy. Chest. 1992; 102: 1716-22. [PMID: 1446478] 10. Chaudhuri A, Behan PO. In vivo magnetic resonance spectroscopy in chronic fatigue syndrome. Prostaglandins Leukot Essent Fatty Acids. 2004; 71: 181-3. [PMID: 15253888] 11. Jones DE, Hollingsworth KG, Taylor R, Blamire AM, Newton JL. Abnormalities in pH handling by peripheral muscle and potential regulation by the autonomic nervous system in chronic fatigue syndrome. J Intern Med 2010; 267: 394-401. [PMID: 20433583]	

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				12. Yoshiuchi K, Farkas I, Natelson BH. Patients with chronic fatigue syndrome have reduced absolute cortical blood flow. Clin Physiol Funct Imaging 2006; 26: 83-6. [PMID: 16494597] 13. VanNess JM, Stevens SR, Bateman L, Stiles TL, Snell CR. Postexertional malaise in women with chronic fatigue syndrome. J Womens Health (Larchmt) 2010; 19: 239-244. [PMID: 20095909] 14. Van Oosterwijck J, Nijs J, Meeus M, Lefever I, Huybrechts L, et al. Pain inhibition and postexertional malaise in myalgic encephalomyelitis/chronic fatigue syndrome; an experimental study. J Intern Med 2010; 268: 265-78. [PMID: 20412374] 15. La Manca JJ, Sisto SA, DeLuca J, Johnson SK, Lange G, Pareja J, Cook S, Natelson BH. Influence of exhaustive treadmill exercise on cognitive functioning in chronic fatigue syndrome. Am J Med 1998; 105: 59S-65S. [PMID: 9790484] 16. VanNess JM, Snell CR, Stevens SR. Diminished cardiopulmonary capacity during postexertional malaise. J Chronic Fatigue Syndr 2007; 14: 77-85.	
Physios for ME	Guideline	General	General	We feel that these revised guidelines will have a significant impact on the clinical practice of physiotherapists, with the move away from exercise-based treatments. Given the sparsity of training and education for undergraduate and post-graduate physiotherapists, it will be a challenge to effectively communicate these changes across the profession and make the necessary changes to established physiotherapy services. Physios for ME have developed an initial education package and would be happy to be a part of developing and delivering training provision for physiotherapists going forwards. It will also be essential that the Chartered Society of Physiotherapy supports implementation of appropriate training and educational provision	Thank you for your comment and this information. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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				to reflect the new guidance, as well as a communication campaign to raise awareness of this significant change in clinical practice.	
Physios for ME	Guideline	006 - 007	007 onwards	We support the additional precautions for people with Severe ME, including to risk assess each interaction to ensure benefits outweigh the risks, due to the exacerbation of symptoms that can be caused by cognitive, sensory and physical stimulation. We feel more emphasis should be placed on the need for specialist care for people with Severe ME. An MDT should be led by a practitioner with an interest and specialism in severe ME as a neurological disease, and the team should include specialist severe ME nurses, dieticians, physiotherapists and occupational therapists. Support should be given for family and carers due to the extreme isolation that can occur.	Thank you for your comment. *MDT* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. In addition, the committee discussed the value of naming which professionals should be in a team and as you comment no list is ever satisfactory or agreed. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care) The committee note that throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. For people with severe and very severe ME/CFS access to physiotherapists and occupational therapists working within ME/CFS specialist teams and to dieticians with a special interest in ME/CFS is recommended. *Support for family and carers* The committee agree support is very important and have reinforced this throughout the guideline and link to the NICE guideline on supporting adult carers on identifying, assessing and meeting the caring, physical and mental health needs of families and carers.

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					To note after considering stakeholder comments the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline.
Physios for ME	Guideline	005	012	We support the importance of more regular monitoring for people with ME as opposed to one-off blocks of "treatment", as this reflects the long-term fluctuating nature of ME and the need for long term support.	Thank you for your comment.
Physios for ME	Guideline	008	017	Box 1- We support Post Exertional Malaise being emphasised as a defining feature. With regards diagnostic criteria we would therefore recommend that NICE highlight criteria that include Post Exertional Malaise, and identify those that do not (as stipulated in Evidence Review D - Diagnosis) so that appropriate diagnostic criteria can be applied both clinically and in future research studies	Thank you for your comment. The symptoms are all required for suspecting ME/CFS and are not in any order of priority. As you note the committee do highlight the criteria that include Post Exertional Malaise, and identify those that do not in Evidence Review D – Diagnosis. Recommendation 1.2.4 sets out the criteria to use for diagnosis.
Physios for ME	Guideline	009	019 - 020	We entirely support the statement that advice regarding symptom management should be given to people as soon as ME/CFS is suggested. However, as with the draft recommendation for children and young people (page 10 1.2.8) we propose this should include that "where ME/CFS is suggested, written advice should be sent to the workplace regarding flexible adjustments or adaptations" We acknowledge that this information is described on pages 21 point 1.9.1 but propose this advice about adjustments and adaptations should be highlighted at the early stages of the development of ME/CFS and should highlight the recommendations 1.3.1 (page 10 lines 15 – 20) about the need to rest and not push through activity.	Thank you for your comment. The committee made specific recommendations for children and young people based on the qualitative evidence (see evidence reviews A and B) and their experience. This was seen as particularly important to recommend at this stage noting the detrimental impact ME/CFS can have on a child or young person's education. The committee note that at this stage ME/CFS is suspected and contact with a person's workplace may result in wrong information being given and when diagnosis is confirmed is a more informed option, for this reason the committee have not added your suggestion.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

Consultation on draft guideline - Stakeholder comments table

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Physios for ME	Guideline	010	009 - 010	We strongly support the need to "write to the child or young person's place of education or training to advise about flexible adjustments or adaptations." to avoid any disruption to education as described on page 50 lines 13 – 15. We acknowledge that this information is described on pages 21/2 points 1.9.4 – 1.9.6 but propose this early advice about adjustments and adaptations should also highlight the recommendations 1.3.1 (page 10 lines 15 – 20) about the need to rest and not push through activity due to the cognitive and physical demands posed by participation in educational activities. We also feel that in line with the Department of Education's statutory guidance for local authorities "Ensuring a good education for children who cannot attend school because of health needs" (2013) this advice should highlight the importance of including social and emotional needs, for example ensuring that pupils feel fully part of their school community, are able to stay in contact with classmates, and have access to the opportunities enjoyed by their peers. Due to the fluctuating nature of ME/CFS, it is important that this advice should include the need for the nature of the provision to be responsive to the demands of what may be a changing health status as described in the Department of Education's statutory guidance for local authorities. These proposals are all supported by the themes arising in the NICE supporting document "Children and Young People" which highlight the need for flexible educational provision and the importance of maintaining social relationships whilst trying to balance energy expenditure and avoiding symptom exacerbation.	Thank you for your comment. The committee agree early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and allows for further communication when the diagnosis is confirmed. At this stage the support to the child's or young person's place of education should be specific to their current circumstance and condition.

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Physios for ME	Guideline	013	012	We agree that home visits should be offered to people with Severe ME due to the nature of this disease meaning patients are often completely bedbound and therefore unable to access services outside of their home. We would also suggest that home visits should be offered to those with mild-moderate ME given the energy expenditure required to attend a session, which may trigger Post Exertional Symptom Exacerbation and deter patients from seeking advice and help from services. We therefore would recommend all ME services offer a range of delivery mechanisms for assessment and ongoing monitoring, including home visits and use of virtual consultations where appropriate.	Thank you for your comment. *Home visits* The committee agreed that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Physios for ME	Guideline	016	006 - 011	We agree with comments by Forward ME regarding this: Replace 2 paragraphs with the following: 1.7.1 Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect. In the case of children, ME/CFS should not be mistaken for very rare conditions such as Munchausen's syndrome by proxy or with fabricated or induced illness. 1.7.2 Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out and overseen by health and social care professionals who have training and experience in ME/CFS.	Thank you for your comment. Taking into account the range of stakeholder comments the recommendations in this section have been reordered. This has addressed the point you make about the order. The committee discussion in Evidence review B includes in detail why the recommendations on safeguarding have been included in the guideline and this refers to the lack of understanding and disbelief that parents have experienced.
Physios for ME	Guideline	018	010	We strongly support that someone with ME should not be discharged due to missing an appointment. This practice fails to acknowledge the variability of the disease and punishes those suffering a flare-up.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
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Physios for ME	Guideline	022	013 - 016	ME/CFS is a complicated, multi-system, chronic medical condition and we agree that patients should be supported by multi-disciplinary teams. We do not feel it is appropriate for specialist ME/CFS services to be led by Psychiatrists or Psychologists as is often currently the case in the UK.	Thank you for your comment and this information.
Physios for ME	Guideline	022	010 - 012	We support that children should be advised to find a balance between education and social/family life. This is supported by the Department of Education's statutory guidance for local authorities ("Ensuring a good education for children who cannot attend school because of health needs" (2013)) which highlights the importance of social and emotional needs, for example ensuring that pupils feel fully part of their school community, are able to stay in contact with classmates, and have access to the opportunities enjoyed by their peers. It is also supported by the themes arising in the supporting document "Children and Young People" which highlight the need for flexible educational provision and the importance of maintaining social relationships whilst trying to balance energy expenditure and avoiding symptom exacerbation.	Thank you for your comment.
Physios for ME	Guideline	024	014 - 015	Include mention of "post exertional symptom exacerbation" to reemphasise that this is the hallmark symptom and energy management is designed to avoid this and to keep below the threshold that triggers it.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits'.
Physios for ME	Guideline	024	010	We strongly support that it is important to make the distinction that energy management is a maintenance strategy, not a "treatment" strategy	Thank you for your comment.

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Physios for ME	Guideline	025	027 - 029	We agree with this statement and would add that although there is limited evidence for heart rate monitoring at present, the Workwell Foundation has produced guidelines for the use of HR monitoring based on clinical testing of over 100 patients with ME/CFS (https://www.dialogues-mecfs.co.uk/films/pacing/). In addition, people with ME/CFS themselves have set up facebook groups (ME/CFS, pacing with a heartrate monitor #2) with several thousand followers who advocate for and regularly use heart rate monitoring to manage their symptoms.	Thank you for your comment. In the rationale section the committee recognise there was a lack of effectiveness evidence on tools to support people to self-monitor activity management. The committee decided to recommend that activity recording should be as easy as possible, and people should take advantage of tools they are already using and gave examples of these. The committee also decided to make a recommendation for research on self-monitoring management strategies to help determine which techniques are effective.
Physios for ME	Guideline	025	025 - 026	More emphasis should be placed on management of flares. We would recommend expanding this paragraph to include more information from, or a signpost to, the "Managing Flares and Relapse" section on page 37	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'
Physios for ME	Guideline	025	021	Change the sentence "alternate and vary between different types of activity and break activities into small chunks" To: "Alternate and vary between different types of activity, for example cognitive activities or physical activities, and break them into small chunks to avoid triggering Post Exertional Symptom Exacerbation." This will emphasise that activity can be both cognitive and physical, and both types can cause exacerbation of symptoms.	Thank you for your comment. After considering the stakeholder comments the first recommendation of the principles of energy management was edited to clarify that this includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. **As this is now clarified here your point has not been added to this recommendation.**
Physios for ME	Guideline	026	001 - 007	We are concerned about the bullet points regarding referring someone to a specialist service if they: • are ready to progress their physical activity beyond their current activities of daily living	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'.

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				• would like to incorporate a physical activity programme into the management of their ME/CFS To suggest someone will be "ready to progress" their physical activity could provide impetus to instigate a progressive exercise programme. The terminology also suggests a person can achieve increased physical activity when "ready" and leaves open interpretation as to who can make this judgement, without any guidance on how or on what basis. To suggest that a physical management programme could be part of the management of ME contradicts the guideline's recommendation not to offer any therapy based on physical activity or exercise as a treatment or cure, due to the low to very low quality of evidence of clinical effectiveness and qualitative evidence of harm. "Physical activity", as defined by this guidance document, is "any bodily movement produced by skeletal muscles that results in energy expenditure." This therefore includes a wide range of activities, both general activities of daily living as well as any physical activity that the person wishes to pursue within the confines of their energy envelope without triggering Post Exertional Symptom Exacerbation. The management of physical activity is included within an energy management plan, with guidance provided in the "Energy Management" section on page 24 of the NICE Guidance. Therefore our suggested wording would be to refer someone to a specialist service if they: - Require support with activity and energy management planning	Based on the quantitative and qualitative evidence and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service

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				This would allow a therapist to work with a patient in planning out their daily activities – which could include physical activity – but in a manner that fits their available energy envelope	The energy management plan is initially developed as part of the care and support plan by the ME/CFS specialist team, these recommendations are to ensure that people are directed to physiotherapists or occupational therapists for specific support.
Physios for ME	Guideline	026 027	022 002	A physical maintenance plan should be developed based on severity of ME and with the aim to avoid Post Exertional Symptom Exacerbation. With regards the proposed physical maintenance section of the management plan for people with ME/CFS, we would recommend replacing the bullets: • muscle strength and endurance • cardiovascular health. With the following: - Maintenance of muscular strength to support activities of daily living to the best of the patient's abilities - Maintenance of cardiovascular health to the best of the patient's abilities while staying below their anaerobic threshold. This would emphasise the importance of maintenance, as opposed to suggesting that work on muscular strength and cardiovascular fitness – which is rooted in progressive exercise – should be undertaken	Thank you for your comment. After considering the stakeholder comments, 'Include strategies to maintain and prevent deterioration of physical functioning and mobility in the care and support plans for people with ME/CFS. Strategies may need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the care and support plan and the priorities and symptoms that people may have. In addition, the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. 'Strength and endurance' has been edited to 'muscle function'. The committee considered that cardiovascular health was an appropriate description and have not edited this bullet point.
Physios for ME	Guideline	027	014 - 019	We recommend changing the wording of this paragraph to highlight the importance of knowledge about Post Exertional Symptom Exacerbation. "Give families and carers (if appropriate) advice and support on how to help the person with ME/CFS follow their energy management plan in relation to physical maintenance and mobility. This would include;	Thank you for your comment. This recommendation specifically refers to tasks that the person with ME/ CFS may need support with and as such information on PEM is not relevant here.

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				- Providing information about Post Exertional Symptom Exacerbation and the importance of avoiding this - Providing help and guidance in monitoring strategies (for example use of Heart Rate Monitors) to monitor symptoms. - Emphasise that simple activities of daily living, for example; bed mobility, moving from lying to sitting to standing, transferring from bed to chair, use of mobility aids, walking, joint mobility, muscle stretching, muscle strength, balance, and going up and down stairs, may all contribute to Post Exertional Symptom Exacerbation and must be carefully monitored and paced in accordance with the person's energy management plan.	
Physios for ME	Guideline	027	021 - 023	We strongly agree that people with ME should not be told to go to the gym or exercise more because of the abnormal physiological response to exertion as shown in the references in comment 3	Thank you for your comment.
Physios for ME	Guideline	028	001 - 011	We strongly support that NICE are advising against the use of structured exercise programmes and that they are not to be offered as a treatment or a cure, considering the evidence review by NICE of non-pharmacological management for ME/CFS found the quality of evidence of the clinical effectiveness of graded exercise therapy ranged from low to very low, and the range of evidence demonstrating the abnormal physiological response to exertion.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Physios for ME	Guideline	028 029	023 - 029 001 - 005	We recommend removal of this section completely. As earlier in the guidelines has stated; - physical activity is not curative or a treatment, - a defining symptom of ME/CFS is post exertional symptom exacerbation Therefore recommending physical activity programmes is inappropriate.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise

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				"Physical activity", as defined by this guidance document, is "any bodily movement produced by skeletal muscles that results in energy expenditure." The management of physical activity therefore is already included in the energy management plan, and the guidance included in the "Energy Management" section on page 24 of the NICE Guidance. We would also recommend the guidance makes clear that the means to measure post exertional symptom exacerbation must be put in place prior to any new activity being introduced, and if progression is considered then monitoring is essential to avoid exceeding the anaerobic threshold and associated post exertional symptom exacerbation.	programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Physios for ME	Guideline	028	012 - 015	We are concerned about the wording of this paragraph. To suggest someone will be "ready to progress" their physical activity could provide impetus to instigate a progressive exercise programme. The terminology also suggests a person can achieve increased physical activity when "ready" and leaves open interpretation as to who can make this judgement, without any guidance on how or on what basis. To suggest that a physical management programme could be part of the management of ME contradicts the guideline's recommendation not to offer any therapy based on physical activity or exercise as a treatment or cure, due to the low to very low quality of evidence of clinical effectiveness and qualitative evidence of harm.	Thank you for your comment. After considering stakeholder comments this bullet point has been edited to,' feel ready'. Based on the quantitative and qualitative evidence (evidence reviews A, G) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into

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				Suggested alternative wording would be: Only consider physical activity for people with ME/CFS as part of a maintenance plan for activity and energy management to support activities of daily living. The means to measure post exertional symptom exacerbation must be put in place prior to any new activity being introduced, and if progression is considered then monitoring is essential to avoid exceeding the anaerobic threshold and associated post exertional symptom exacerbation.	managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Physios for ME	Guideline	028	019 - 022	We strongly support that people should be warned of the risks of physical activity, as worsening of symptoms have been repeatedly reported in the qualitative evidence review by NICE of non-pharmacological management for ME/CFS. We recommend removing the word "programme" from physical activity, as this connotes a formal exercise programme, and we know that general physical activity, for example climbing the stairs, can also be enough to exacerbate symptoms.	Thank you for your comment. The programme is part of the care and support plan and the energy management plan, 'programme' is used to illustrate it is addresses physical activity or exercise in particular.
Physios for ME	Guideline	028	016 - 018	We are concerned about the current level of training on ME/CFS for Physiotherapists and Occupational Therapists. Unpublished surveys by Physios for ME found ME was included in less than half of undergraduate physiotherapy courses. Many existing training programmes are based on the deconditioning model and include graded exercise therapy. We therefore recommend changing the wording from: A physical activity programme, if offered, should only be delivered or overseen by a physiotherapist or occupational therapist with training and expertise in ME/CFS.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula. The committee discussed the level of detail that should be included in training programmes and agreed on a general

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				To: "Any physical activity within an activity management plan should be overseen by a physiotherapist or occupational therapist who has undertaken current, evidence-based training in exercise physiology relating to ME/CFS and can evidence their continuing professional development within this speciality. An awareness of the abnormally lowered anaerobic threshold, lowered VO2 max, increased acidosis post-exercise and their implications are essential. Training should reflect the low to very low quality of evidence relating to GET and the additional recent evidence related to adverse physiological responses to exertion and the implications for this on activity management planning."	description to avoid a prescriptive interpretation of the content. This allows the recommendations to remain relevant as research in the area develops.
Physios for ME	Guideline	029	006 - 013	We recommend removal of this section completely. As earlier in the guidelines has stated; - physical activity is not curative or a treatment, - a defining symptom of ME/CFS is post exertional symptom exacerbation Therefore recommending physical activity programmes is inappropriate. "Physical activity", as defined by this guidance document, is "any bodily movement produced by skeletal muscles that results in energy expenditure." The management of physical activity therefore is already included in the energy management plan, and the guidance included in the "Energy Management" section on page 24 of the NICE Guidance. We would also recommend the guidance makes clear that the means to measure post exertional symptom exacerbation must be put in place prior to any new activity being introduced, and if	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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				progression is considered then monitoring is essential to avoid exceeding the anaerobic threshold and associated post exertional symptom exacerbation. We would recommend guidance on flare management be added to the Energy Management section on page 24	*See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). The recommendations include that the plan should include recognising a flare-up or relapse early and outlining how to manage it.. The energy management section of the guideline includes links to the section on flare-ups and relapses.
Physios for ME	Guideline	030	003 - 012	We welcome inclusion of information regarding orthostatic intolerance but feel more details should be included, for example how to recognise this condition. The guidelines should recognise that while physical activity is useful in the management of orthostatic intolerances, the priority of management should always be on avoiding post exertional symptom exacerbation, and therefore cardiovascular training used for orthostatic intolerances is not appropriate for people with ME/CFS.	Thank you for your comment In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance. The managing co-existing conditions of section of the guideline recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
Physios for ME	Guideline	030	013 - 016	The pain guidelines referenced here are appropriate. We recommend that NICE recognise that while physical activity can be useful in the management of persistent pain, the priority	Thank you for your comment. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people

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				of management should always be on avoiding post exertional symptom exacerbation, and therefore treatment should be adapted for people with ME/CFS.	with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS.
Physios for ME	Guideline	034 035	001 - 030 001 - 026	We agree with the comments made by Forward ME regarding this: In the evidence review at G Page 342 Line 26, the committee summarised the evidence on non-pharmacological interventions for ME/CFS. Their conclusions (from lines 40 – 44) found that: "In addition, the committee made 'do not' offer recommendations for CBT ………to treat or cure ME/CFS." In the light of this finding, Forward-ME are mystified as to why the draft guideline discusses CBT extensively. This would appear to be discriminatory as the guideline for multiple sclerosis (MS) – a disease that has been compared to ME/CFS, at 1.5.5 states only: 'Consider mindfulness-based training, cognitive behaviour therapy or fatigue management for treating MS-related fatigue. Congestive heart failure- also compared with ME/CFS only makes reference to Depression with reference to the NICE guideline on that topic. We can find no other chronic disease for which such extensive advice is given on CBT. We are aware that some patients may find psychological support necessary and helpful. We are asking for this section to be re-written to state: 'Do not offer CBT to treat or cure ME/CFS as there is no substantive evidence that it is effective. Patients may find supportive counselling helpful.'	Thank you for your comment. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *Treatment or cure* To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
Physios for ME	Guideline	036	001 - 021	Managing co-existing conditions. The guidelines should recognise that while physical activity is useful in the management of most co-existing conditions, the priority of management should always be on avoiding post exertional symptom exacerbation, and therefore treatment should always be adapted for people with ME/CFS	Thank you for your comment. The first two recommendations in this section address this and advise that when managing coexisting conditions in people with ME/CFS, the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account.
Physios for ME	Guideline	040	011 - 023	We strongly agree that training should be provided for all health and social care staff who deliver care to people with ME/CFS. Given the wide number of professionals potentially involved in the care and management of people with ME, both for their ME and for other co-morbidities, it is essential that training forms part of core curriculum provision for doctors and AHPs, including physiotherapists, OTs and nurses. Unpublished surveys by Physios for ME found ME was included in less than half of undergraduate physiotherapy courses. Many existing training programmes are based on the deconditioning model and include graded exercise therapy. With the emphasis on earlier recognition of ME/CFS and advice for people with suspected ME/CFS, it is also essential that GPs and other primary care staff receive training in the recognition and diagnosis of ME/CFS. This will be challenging to implement but has the potential to significantly improve diagnosis, care and management and improved outcomes for people with ME. The Royal College of General Practitioners should ensure this is embedded in delivery of training and education for future GPs and those who are already working in general practice. Any training on ME must be based on the current evidence in exercise physiology relating to ME/CFS.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content. This allows the recommendations to remain relevant as research in the area develops.

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				Training must reflect the low to very low quality of evidence relating to GET and the additional recent evidence related to adverse physiological responses to exertion and the implications for this on activity management planning.	
Physios for ME	Guideline	041	General	We have concerns regarding the definition and use of terms that have been used in a particular way in this guidance, namely: - "Activity" (any effort that uses energy) - "Physical Activity" (defined as a sub-category of activity) - "Exercise" (defined as a sub-category of physical activity) - "Physical maintenance" (which may include physical activity) Given the complexities of these definitions and how the terms can easily be used in different contexts in pre-existing clinical discourse, we feel more emphasis should be placed on how the terms are used in a particular way in this document and the full definitions stated within the guidance document, rather than solely on the back pages, so that any health professional using the guidance as a quick point of reference can fully understand the information presented without having to cross-reference terminology.	Thank you for your comment. The committee agree it is important to include these definitions with reference to ME/CFS and to provide some clarity on the differences in the terms (for example physical activity and exercise). However when writing recommendations there is a fine line between reinforcing information and repeating information in the text of the recommendations. Too much detail and repetition results in a guideline becoming unwieldy and unusable. For this reason the detail of the definitions has been kept in this section of the guideline.
Physios for ME	Guideline	044	016 - 017	Change: "Such activity is undertaken within the person's energy envelope and avoids pushing through boundaries of tolerance." To: "Such activity is undertaken within the person's energy envelope and avoids triggering post exertional symptom exacerbation".	Thank you for your comment. The committee agreed that your suggestion did not add any further clarity to the definition and have not made these changes.
Physios for ME	Guideline	045	008 - 010	We strongly support the research recommendation regarding the clinical and cost effectiveness of self monitoring techniques in guiding energy management in ME/CFS. The qualitative accounts from people with ME consistently describe the benefits of these approaches and therefore further	Thank you for your comment.

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				investigation is essential to advise and guide both health professionals and patients	
Primary Care Rheumatology and MSK Medicine society	General	General	General	I read half of this and struggled to find any evidence for diagnostic criteria. Then I reached the paragraph about people being unlikely to have persisting viral symptoms for more than 6 weeks after a virus and immediately the guideline is out of date because if Long-covid. Everyone with long-covid could be thought of as having MR/CFS according to this guideline so it is inaccurate and not really fit for purpose because of COVID.,	Thank you for your comment. The evidence for the diagnostic criteria is set out in Evidence review D_Diagnosis. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. The period of a minimum of 6 weeks is to alert clinicians to the possibility of ME/CFS, diagnosis is not considered until symptoms have been persistent for 3 months and other conditions have been excluded. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 list the common symptoms of ongoing symptomatic COVID-19 and post-COVID-19 syndrome. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms than in the diagnostic criteria in the ME/CFS guideline. The key difference being the presence of post exertional malaise as a key criteria in people with ME/CFS.
Primary Care Rheumatology and MSK Medicine society	General	General	General	It's difficult to see who was involved in writing the draft guidance. Who were they? What is their link to ME/CFS? Do they have any conflicts of interest or bias? (Did I miss this info somewhere??)	Thank you for your comment. This information is included in the project documents of the Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management page on the NICE website. https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents
Primary Care Rheumatology and MSK Medicine society	General	General	General	It is acknowledged within the draft that there is little evidence on which to base guidance, therefore it would seem important that the wording of the guidelines reflects this, and that firm directives cannot be made only suggestions. Yet throughout the guidance	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of

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				are very didactic statements telling clinicians what to do. Many examples e.g.	stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Primary Care Rheumatology and MSK Medicine society	General	General	General	There are recommendations that the lighting, sounds and smells within a clinical environment should be modified to accommodate the person with CFS/ME. The environment however reflects the safe assessment and care given to other groups of patients. This again therefore should be worded as 'desirable' only. Recommendations for home visits ditto.	Thank you for your comment. These factors (including home visits) were identified in Evidence Review C_ Access to care, Appendix 2 and by the committee as important to enable people with ME/CFS to access health and social care services. Without these adaptions some people with ME/CFS are unable to successfully access services. As you note the environment reflects the safe assessment and care given to other groups of patients and an appropriate environment should be equally available to people with ME/CFS. Home visits

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					The symptoms experienced by people with ME/CFS can mean that physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. The committee agreed that flexibility in accessing services is important to address these barriers to care. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agree that there is variation in the delivery of home visits across the NHS but these recommendations will provide equity of access for this group, particularly for people with ME/CFS who are have difficulty or are unable to leave their homes.
Primary Care Rheumatology and MSK Medicine society	General	General	General	Also regarding work and education establishments. There is little acknowledgement that this type of activity generally lies outside the GP contract. For example.	Thank you for this information.
Primary Care Rheumatology and MSK Medicine society	General	General	General	Not really my area of expertise, but I have read through the document and here are my observations. • It clearly identifies the benefit of early diagnosis, how it manifests and defines it well as a medical condition that should be taken seriously. This comes across strongly which is good. • The document is very clear, avoiding unnecessary jargon and waffle. • What comes across strongly is a holistic approach and personalised care planning which is great. Involvement of family is also considered which is important.	Thank you for your comments.

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				• The guidance provides very good links to patient information which is so important in patient engagement. • The information for young people is thorough, considered and clear. Very good. Safeguarding issues dealt with. • I particularly like how the guidance realises what situations are likely to be challenging for ME patients such as going into hospital, the workplace and education. This has been thought through. • The advice on management strategies is comprehensive, clear and doesn't appear contencious. Overall, as a clinician looking from the outside in, it is very easy to read/follow.	
Primary Care Rheumatology and MSK Medicine society	General	General	General	Another thing that troubles me regarding the lack of evidence in this draft, is the compelling evidence FOR the benefits of exercise in almost all other populations and illnesses studied. To single this group out without evidence of harm from exercise and then claim they cannot derive the benefits that everyone else does, may make clinicians complicit in encouraging further harm. That's not right surely.	Thank you for your comment. It is commonly agreed that people with ME/CFS can experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living

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					- would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS.
Primary Care Rheumatology and MSK Medicine society	General	General	General	As ? Fiona Godlee says, if you don't know the answer it's better to say nothing (or something like that!)	Thank you for your comment.
Primary Care Rheumatology and MSK Medicine society	General	General	General	I am concerned that we have a very complex and obviously time consuming guideline for a condition that we have no definitive criteria for diagnosing. Reading their section on diagnosis, I find it very difficult to differentiate what they define as CFS/ME from fibromyalgia. This has significant implications for patients, their management, service provision and resources. I would feel that getting a diagnosis of fibromyalgia would make you a second class citizen and I could see that patients with fibro would be clamouring for a diagnosis of CFS/ME. The guideline feels as if it's come from a very biased viewpoint - it seems very negative about a lot of our core treatments that we use for many different conditions, and in particular treatments that we use for fibromyalgia which seems very confusing given the obvious overlap. I found the evidence base across the board for interventions appeared to be very variable but generally of poor quality with low numbers of patients involved. It does not seem to be of good enough quality to make such strong negative statements.	Thank you for your comment. *Fibromyalgia* Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated. *Decision making and strength of the recommendations* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be

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					covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Primary Care Rheumatology and MSK Medicine society	Guideline	011	007	1.4.2 1). Early referral to "specialist teams" experienced in the management of CFS / ME recommended after patient has experienced symptoms for 4-6 weeks,depending on age (1:4:2).We have no such resources available locally.Such patients are referred to rheumatology (frequently with the GP having already diagnosed ME / fibromyalgia already),investigated for alternative diagnoses & discharged back with a recommendation that they be referred to psychology / IAPT for CBT or,if merited by virtue of the overall level of mental / physical disability,Liason Psychiatry.So,this recommendation is utterly unhelpful in the absence of any alternative recommendations.	Thank you for your comment. People are referred at 3 months to ME/CFS specialist teams. At 6 weeks adults with suspected M/CFS are given advice and children and young people at 4 weeks are referred to a paediatrician for further assessment and investigation for ME/CFS and other conditions.
Primary Care Rheumatology and MSK Medicine society	Guideline	013	012	1.5.5 Encouraging home visits for those adjudged to be suffering from severe CFS/ME (1:5:5) is understandable but,even in a post-COVID era,something I see as difficult to implement,especially if this is seen to contribute to a complex	Thank you for your comment. *Home visits* The committee agreed that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be

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				behavioural trait which incorporates elements of acquired helplessness.	difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. This recommendation is directed at assessment and development of the care and support plan. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the assessment and development of the care and support plan but other methods may be more appropriate depending on the person's symptoms.
Primary Care Rheumatology and MSK Medicine society	Guideline	015	016	1:6:9 Similarly,asking primary care workers to undertake referrals to social services on behalf of the patient (1:6:9) risks removing an element of personal responsibility in the management of a condition which requires a collaborative approach between the Primary Care Team (PCT) & the patient.The PCT should signpost to resources but,thereafter,it's up to the patient and their carer(s) as to how they wish to proceed.	Thank you for your comment. The committee agree and the first part of the recommendation is to support someone to self-refer, the offer to refer is to support people with ME/CFS who have additional needs and are unable to self-refer.
Primary Care Rheumatology and MSK Medicine society	Guideline	016	012	1.7.3 - If an assessment under the Mental Health Act 1983 or the Mental Capacity Act 2005 is needed, involve health and social care professionals who have training and experience in ME/CFS. This should be done within 15 24 hours in an emergency. *This is unlikely to be possible often and the wording should be altered to make this desirable not a necessity in the current NHS.*	Thank you for your comment. After considering the stakeholder comments the reference to 24 hours has been removed to acknowledge the involvement of health and social care professionals with ME/CFS may be later in the process.

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Primary Care Rheumatology and MSK Medicine society	Guideline	019	001	1:8:5 Patients requiring inpatient care being able to manage their inpatient environment (single room,dimming of lights,noise reduction measures, etc..) strikes me as aspirational at best but extremely difficult to achieve,even in a post-COVID healthcare setting (1:8:5).	Thank you for your comment. The committee acknowledge that these aims and adaptions may not always be achievable but they should be considered and addressed where possible to improve access to care for people with ME/CFS.
Primary Care Rheumatology and MSK Medicine society	Guideline	021	011	1.9.2 Offer to liaise on the person's behalf (with their informed consent) with employers, education providers and support services. *The guidance needs to acknowledge that the ability to work is carried out by occupational health departments, and is otherwise not part of core NHS activities.*	Thank you for your comment. The committee disagree in their experience they do liaise with employers, education providers and support services and this can involve occupational health departments.
Primary Care Rheumatology and MSK Medicine society	Guideline	025	015	1.11.4 4 Based on the person's assessment, establish an individual activity pattern within their current energy envelope that minimises their symptoms. For example: • reduce activity as the first step. *Where is the evidence for this statement?*	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
Primary Care Rheumatology and MSK Medicine society	Guideline	028	012	1:11:17.I question the practicality of relying solely on the patients' readiness to progress their physical level as part of their rehabilitation as opposed to a graded exercise programme or equivalent (1:11:17).Patients frequently lack the motivation / desire to progress & while recognizing that 'you can drag a horse to water,etc..',surely being gently directive in providing instruction / advice is not unreasonable here.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. Alongside this the committee recognise the importance of having a collaborative supportive, trusting and empathetic relationship with people with ME/CFS.

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Primary Care Rheumatology and MSK Medicine society	Guideline	028	016	1:11:18 The idea that "only" specialized OTs / physios should be responsible for the provision of exercise / rehabilitation instruction is fanciful (1:11:18).Personally,I had no idea such super-specialized professionals exist.	Thank you for your comment. The committee note that there are occupational therapists and physiotherapists that work in ME/CFS specialist teams and have the specialist skills described in the guideline.
Primary Care Rheumatology and MSK Medicine society	Guideline	031	010	1.11.31 Take into account when prescribing that people with ME/CFS may be 11 more intolerant of drug treatment and have more severe adverse effects. Consider: • starting drug treatments at a lower dose than in usual clinical practice • gradually increasing the dose if the drug is tolerated. *Where is the evidence?*	Thank you for your comments. After considering the stakeholder comments the committee agreed to delete 'and have more severe adverse effects' but have retained the information that people with ME/CFS maybe less tolerant of drug treatment. The committee agreed that in their clinical experience and consensus view intolerance of drug treatment was not uncommon in people with ME/CFS and prescribers should take this into account when starting drug treatments.
Primary Care Rheumatology and MSK Medicine society	Guideline	034	006	1:11:44 Again,CBT being provided "only" by practitioners specializing in the management of ME/CFS (1:11:44) cannot be practical,surely.Desirable,yes,but our NHS economy is not able to support this kind of recommendation.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.
Register of Lightning Process Practitioners	Appendix 1 – Children and young people	009	022	2.5.3 sampling Sample size Comments: The sample is described as heterogenous. This statement needs to be further qualified. Did it include those who have recovered? If not, it cannot be seen as representative of the entire population of those dealing with ME/CFS.	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition

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					severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). In addition, the qualitative reviews across the guideline included the views of a wide range of people, including people who have improved or recovered and those who are still affected by ME/CFS. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
Register of Lightning Process Practitioners	Appendix 1 – Children and young people	007	007	2.1 Abstract 2.1.1 Background Comment: It is reassuring to find the views of those receiving care is being included in the process of creating the guideline. However, the	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party

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				methodology for discovering those views need to include those who have recovered as well as those still affected by the illness. Without this, a complete view of how the illness affects people's lives cannot be ensured.	organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). In addition, the qualitative reviews across the guideline included the views of a wide range of people, including people who have improved or recovered and those who are still affected by ME/CFS. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
Register of Lightning Process Practitioners	Appendix 1 – Children and young people	009	037	2.3.4 Recruitment and procedures The recruitment through the Action for ME member directory, website and social media pages, uses a single charity as a sampling source and as identified in Evidence G, this selective	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and

				source renders it prone to bias. Those who have recovered are unlikely to continue to be members or visit a website or social media of an organization supporting those with the illness.	the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). Section 4 of Appendix 1 describes the committee's overview of the consultation. In this they noted it was unclear if all the sample were recruited from Action for ME potentially representing only one group of young people with similar views and if the participants were currently under NHS care and if the experiences reflected current care.it was unclear if the participants were currently under NHS care and if the experiences reflected current care. This was taken into account in the committee's decision making when considering how this contributed to the body of evidence and when making the recommendations. In addition, the qualitative reviews across the guideline included the views of a wide range of people, including people who have improved or recovered and those who are still affected by ME/CFS. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that

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					were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	General	General	This is an excellent project. Discovering people experiences of the illness is essential for developing solutions to help them. There does seem to be one major omission, which is the inclusion of those who have had the illness and recovered, instead of using just the voice of the patients who have not recovered. It would seem valuable to have had the input of those ME/CFS patients who have recovered to provide a more complete narrative on the range of experiences with the illness. Without it, this balance the findings fail to represent the experience of all those with severe ME/CFS.	Thank you for your comment. The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS. The study authors set out the limitations of the consultation acknowledging that patients who have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in this type of studies. This committee took this into account in the decision making.
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	007	035 - 038	60 complete responses, including meeting our inclusion criteria of self-reported severe status and ME/CFS confirmed by a medical professional. Comment: This is a small response rate from the 1600 initially interested in taking part and raises questions about how representative the sample is of the population.	Thank you for your comment. In Appendix 2 the study authors set out the limitations of the consultation and acknowledge the difficulties in recruiting people with severe ME/CFS to a study and the representation of the sample. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making.
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	007	034 - 035	'using social media promotion and advertising via patient organisations' Comment: This approach makes the inclusion of any who have recovered unlikely (as mentioned elsewhere in the documentation) and provides a limited and unrepresentative data set of all those who have had (i.e. currently have or are now recovered) severe ME/CFS.	Thank you for your comment. The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS. The study authors set out the limitations of the consultation acknowledging that patients who have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in this type of studies. This committee took this into account in the decision making.

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Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	010	002 - 003	'The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS' Comment: Unfortunately, the aim of the project limits the range of information that can be discovered about the journey of those with severe ME/CFS as it excludes those with ME/CFS who have recovered from the condition.	Thank you for your comment. As you note the aim of this project was to recruit and explore the opinions of people who have severe ME/CFS. People with severe ME/CFS were specifically identified by stakeholder as underrepresented in the published evidence. The study authors set out the limitations of the consultation acknowledging that patients who have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in this type of studies. This committee took this into account in the decision making.
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	015	006 - 009	twitter open-survey and targeting of charity groups, Comment: This source of participants is unlikely to recruit those who have had the illness and recovered (as noted elsewhere in the NICE evidence documents). It would seem valuable to have had the input of those ME/CFS patients who have recovered to provide a more complete narrative on the range of experiences with the illness. Without it, this balance the findings fail to represent the experience of all those with severe ME/CFS.	Thank you for your comment. The aim of this project was to recruit and explore the opinions of people who have severe ME/CFS. People with severe ME/CFS were specifically identified by stakeholder as underrepresented in the published evidence. The study authors set out the limitations of the consultation acknowledging that patients who have recovered from ME/CFS or who have moved from severe to moderate or mild symptoms might be unwilling to engage in this type of studies. This committee took this into account in the decision making.
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	016	033	1600 clicked and opened survey, 124 completed, 60 self-reported clearly as severe Comment: This low response rate unfortunately makes the representativeness of the sample questionable	Thank you for your comment. In Appendix 2 the study authors set out the limitations of the consultation and acknowledge the difficulties in recruiting people with severe ME/CFS to a study and the representation of the sample. In section 4 of the appendix the committee also noted the sample was a self-selected group and the diagnosis was self-reported sample and this was taken into account in the decision making.
Register of Lightning Process Practitioners	Appendix 2 – People with severe MECFS	031	020	I was also told … that out of all the alt therapies the lightning process was the most promising. Which seems ridiculous knowing what I now know." Comment: This response is an excellent example of the theme of misunderstandings about the nature of the LP intervention present throughout the NICE documentation. The published	Thank you for your comment. This was a quote from one of the respondents about the advice they were given from their GP and then their view. It is not clear where the participant got their information from.

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				evidence does not support this person's opinions and unfortunately identifies they are gaining information from sources not referencing the evidence base.	
Register of Lightning Process Practitioners	Appendix 3 - Expert testimonies	007		Conflict of interest/Lack of impartiality - Jonathan Edwards- Expert Testimony: Professor Jonathan Edwards claims to have no conflict of interest or bias. However, he does admit to being a board director for a ME/CFS patient forum (Expert testimony p 13) and this may explain his adoption of a, possibly unconscious, bias as evidenced by this statement: "I think it is important to establish certain simple facts. The Lightning Process is a commercial product whose nature is secret and whose value is unproven – thus qualifying as an 'alternative therapy'. Yours faithfully, Jonathan Edwards, Professor Emeritus, Division of Medicine, University College London" https://www.virology.ws/2020/05/30/trial-by-error-two-letters-to-dagbladet-about-its-me-coverage/. Letters to Dagbladet About Its ME Coverage, 30 MAY 2020: This can also be observed in his desire to devalue the statistically significant result of the SMILE RCT by claiming them to be 'apparent positive results for the Lightning Process'. This inaccurate commentary on the LP, whilst having no direct experience of it or awareness of the published papers or books on it, brings into question his lack of impartiality and his suitability for the role of expert.	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion. The committee acknowledged in his testimony the lack of objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations.
Register of Lightning Process Practitioners	Evidence review G	330 - 331	041 - 053 001 - 023	The committee´s discussion and interpretation of the evidence 3.3 Benefits and harms Qualitative review of other psychological/behavioural interventions Comments: The same issues of selective highlighting of less positive and downplaying of positive findings, inappropriate interpretations of	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the extraction table for this study). Positive accounts of the Lightning

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				the paper and presence of unsubstantiated opinions noted in other sections can unfortunately be identified throughout this section. It does not reflect the way the Reme study (2012) summarised its results: 'Results: Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved. Particularly helpful aspects were the theoretical rationale, practical exercises and the technique they learned. Less helpful aspects were the intensity and short duration of the treatment with little follow-up, the secrecy surrounding it, and feelings of being blamed if the treatment did not work.' Additionally, the phrase 'evidence also showed' (e.g. Evidence also showed that participants were specifically encouraged not to talk to anyone about the therapy), which appears throughout this section, seems an unreasonable way to describe the reported experiences of some (unspecified) of the 9 participants (seven of whom were very satisfied and improved by the intervention). A more accurate description of the paper would be 'some reported that they felt'. In the later description of the Beasant study (2013), the language used by the committee becomes more representative of that paper describing the experiences of the participants as, 'Evidence identified in children/young people with mild/moderate severity ME/CFS showed some found specialist medical care to be positive… Some people reported that… Mothers also noted that' This lack of consistency in the way the different ways the findings of these two papers have been represented and interpreted is of concern and should be reviewed. Detailed comments:	Process emerging from the Reme study have been synthesised and contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist' where descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. The committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Statements emerging from the studies including those reflecting a pressure to be happy and the encouragement not to talk about the therapy have therefore been taken into consideration as they are evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process, raised the committee's concerns and they considered this to raise an important ethical consideration that should be highlighted. We have no evidence to suggest that 81% of people no longer had issues and even then the percentage of people that still appear to be experiencing concerns is not negligible. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the

				Relationship with the therapist Comment: • The table notes that 'Therapists and staff were mostly described as positive and encouraging. There were different opinions about the therapists.' A positive relationship with a therapist is an essential component of any intervention and in some cases, as with any other intervention, this was not achieved. This does not identify that the intervention causes 'harm' or that that type of relationship experience can be generalised to the LP intervention as a whole. • The suggestion that the LP doesn't encourage debate, pressures people 'to be happy all the time and not express any negative feelings' or that it blames them for not getting well is not representative of the LP approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why blame can have no part in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. • It is reported that 7 were much improved and 2 were not. However, it is unclear from the paper to what extent and how many of the participants experienced these specific issues, which, although disappointing to read, are not part of the LP approach. As such, there is a limit to the generalisability of these unquantified reported negative experiences. • When these points are discussed later in the narrative section, the published information about the LP approach has not been included to provide some balance to the reported experiences by these two dissatisfied participants 13 years ago.	Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. After revisiting all the studies, the Reme study was downgraded for moderate concerns over applicability as, as you state, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making. The Beasant 2014 study that included adolescents taking part in the SMILE trial, was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist

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				This raises questions about how relevant these interpretations of the paper are to the delivery of the LP today and how much they should inform the NICE recommendation process. Dishonesty Comment: • This section is unrepresentative of the paper as the word 'dishonesty' is mentioned twice in the entire paper and not included in the abstract. It is the last negative aspect reported in the paper but in this table, it has been promoted to the second finding. • The claim 'People criticised the <u>impression</u> that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed <u>when they claimed</u> the treatment had a 100% success rate' is misleading. The quote from one of the two dissatisfied participants is 'I <u>think</u> the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011). • When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach. It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence	service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from the Beasant study. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. This section should be revised to express the findings more clearly, for example: 'some felt their practitioner had implied a greater change was possible than was achieved in their case; others reported they were much or very improved. The report notes a survey of LP participants on the LP website found that 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course' Theory Comment: The positive comments in this section, which reported "Learning the theory behind LP" as a helpful aspect, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation. Confusing Comment: This theme is at odds with much of the information in the previous theme, 'The Theory', where the educational experience was deemed valuable by many and needs to be reported within that context. Peer support Comment: The positive comments in this section, which reported one helpful aspect of The Lightning Process was "meeting others with chronic fatigue syndrome", are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation and should be reviewed.	

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				Goal setting Comment: The positive comments in this section are minimised in the narrative sections of the document relating to this study and the LP and as a result, are not reflected in the recommendation. Although there were more helpful aspects reported than less helpful aspects, the review has reported more negative findings which do not reflect the study (Reme et al, 2012). This shows a bias in the review of this qualitative study that needs addressing. Practice and application Comment: The positive comments in this section, which reported that the “practical assignments” and “practicing the process” were helpful, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation. Intensity Comment: This interpretative statement ‘The length of the sessions was thought to be too long and intense’ does not reflect the paper’s finding ‘Most of them found the format acceptable and helpful, but several comments were raised regarding the intensity of the treatment’ and should be changed to reflect the findings more accurately. For context, the LP is often delivered in sessions of 4 hours (Crawley et al., 2018) including breaks as required and is paced and tailored to meet the needs of the individuals attending. This information, available in the published documentation of the process at the time, was unfortunately not reflected in the study. This is compounded by it also not being represented in these documents. This needs to be reviewed and updated.	

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				Follow up Comment: For context, since the publication of the paper and subsequent audit of practitioners' delivery of the LP, it is standard procedure for all practitioners to deliver a minimum of 3 hours follow up. This renders the relevance of these findings from 2007 to be of doubtful use when making recommendations in 2020. Although this is a matter of public record, it has not been recognised or reported in the evidence document, which as a result needs to be reviewed and updated. Effectiveness Comment: The phrasing of this statement, "Some experienced an instant healing; some experienced a gradual improvement that continued after treatment ended and some did not find the treatment helpful." bears little resemblance to the much more positive findings in the study in the original paper they are reported as, "Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved" and "Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better." It is questionable why these positive results have been downplayed in this review. This statement should be rewritten to reflect the study more accurately. Secrecy Comment: This statement from 'a (unspecified) few' of the participants is of concern to the LP as it is the opposite of the LP's position. Researchers, clinicians and family members have always been welcome to observe the LP and there is published information about how the LP works and its entire protocol (Crawley et al.,	

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				2018; Parker, 2011, 2013, 2020; Parker et al., 2018). It is standard practice to require any LP participant under 16 to be accompanied by a parent/responsible adult, as evidenced in the RCT (Crawley et al., 2018), and in that study audio recordings were made of the sessions for qualitative analysis. In light of these documented facts, it is clear the LP encourages openness and transparency, and additionally, as the LP is patient-centred there could be no therapeutic value in asking for elements to be kept secret. Additional note: As a result of this study, an audit of how practitioners were delivering the information was undertaken and a specific CPD programme was introduced at the time to ensure this message was communicated even more clearly. In the wording 'The secrecy surrounding the Lightning Process' there seems to be a failure of applying scientific rationale. It is not appropriate to use the experiences reported by '(unspecified) several' of the 9 participants to describe the delivery of the LP in 2007 (when the study was conducted). This should be reflected in this table. It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly post-audit. It is irrational, in light of the evidence of the LP's openness and transparency reported above, to continue to perpetuate these claims of secrecy that circulate on the internet, that can be identified throughout this document and has been central to the drafting of these recommendations. This raises serious concerns about the validity of the recommendations which focus so heavily on this point.	

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Register of Lightning Process Practitioners	Evidence review G	220 - 221	Table 79	2. Experience of interventions 2.1.5 Qualitative evidence synthesis Table 79: Review findings: The Lightning Process (mild/moderate severity) Comment: This qualitative study (Beasant et al., 2013)) is more recent and had a larger number of participants (N = 25) than the Reme study (2012) (Evidence G P 220 Table 78). Participants were asked about their experiences of the interventions which included the LP. Questions asked included: Tell me about the intervention you received? Prompts: What happened? What was good/bad? What would you change? Venue? Structure of sessions? Language used? Was it as expected? No negative responses or harms were reported in the paper, and although this would seem important to note in comparison to the Reme study (2012) this is not presented in the review. This appears to be an inconsistency in the NICE documentation and has affected the recommendation process.	Thank you for your comment. The aim of the Beasant study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process. This limited the extent to which conclusions about the Lightning Process could be drawn from the Beasant study. The study still met the protocol as it included participants from the SMILE trial, some of whom must have received the Lightning Process, depending on which arm they were randomised to and timelines; however, this was not clear from the information reported in the paper. The focus of the paper on specialist services rather than the Lightning Process and the impact of this in the applicability of the findings has been acknowledged in the discussion section of Evidence review G and is also transparent in the assessment of confidence on the findings emerging from this study. Recommendations were made in accordance with *Developing NICE guidelines: The manual* and the methods are further detailed in the methods chapter for this guideline. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When making decisions about interventions the committee take into consideration many factors including the clinical and cost effectiveness, taking into account the benefits and harms, patient experience, equality considerations and as with all NICE guidelines the committee used its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.

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					The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting Process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	192	011	1.1.6 Economic evidence 1.1.6.1 Included studies There is an inconsistency here with LP being included under 'Behavioural/psychological support' and not the Exercise category. Elsewhere it is erroneously included in Physical Activity (e.g. Guideline P 28 L 10). We recommend that this inconsistency is resolved by placing it in either a category of Psychoneuroimmunological approaches, or less accurately, approaches similar to CBT or complementary approaches.	Thank you for your comment. After considering the stakeholder comments the recommendation on the Lightning Process has been moved to a separate subsection in the symptom management for people with ME/CFS section of the guideline.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	2. Experience of interventions 2.1.5 Qualitative evidence synthesis Table 78: Review findings: The Lightning Process General Comments: This table interprets the findings of a qualitative study (Reme et al., 2012), which is used as the primary evidence about the LP throughout the rest of the document. There are issues with this	Thank you for your comment. Evidence identified for the Lightning Process was limited to the included studies by Reme and Beasant. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the

				study's relevance and how it has been reported here and elsewhere in the document. Of particular concern is a downplaying in this review of the key finding that: • Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved. • Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better. • That 7 of the 9 no longer met the criteria for CFS/ME after attending the Lightning Process. There is also a selective highlighting of less positive experiences that is unrepresentative of the paper and a series of misinterpretations of the paper's findings. These concerning issues of bias, detailed in the comments on each section, make the reliance on this interpretation of paper as the primary source of evidence, and a basis for any recommendation, unsound. We would suggest that this table be rewritten in a way which reflects the paper's findings more accurately.	interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the qualitative evidence table for this study). Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist' where descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. In addition to those positive experiences, the committee also considered negative experiences emerging from the study. Statements including those reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Such finding supported the committee's concerns about the Lightning Process. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the

					Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. After revisiting all the studies, the Reme study was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The committee did not dismiss or selectively highlight any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making and as mentioned earlier, there were additional concerns raised which contributed to the current recommendations. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on

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					the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Relationship with the therapist Comment: • The table notes that 'Therapists and staff were mostly described as positive and encouraging. There were different opinions about the therapists.' A positive relationship with a therapist is an essential component of any intervention and in some cases, as with any other intervention, this was not achieved. This does not identify that the intervention causes 'harm' or that that type of relationship experience can be generalised to the LP intervention as a whole. • The suggestion that the LP doesn't encourage debate, pressures people 'to be happy all the time and not express any negative feelings' or that it blames them for not getting well is not representative of the LP approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why blame can have no part in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. • It is reported that 7 were much improved and 2 were not. However, it is unclear from the paper to what extent and how many of the participants experienced these specific issues, which, although disappointing to read, are not part of the LP approach. As such, there is a limit to the generalisability of these unquantified reported negative experiences.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between

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				• When these points are discussed later in the narrative section, the published information about the LP approach has not been included to provide some balance to the reported experiences by these two dissatisfied participants 13 years ago. This raises questions about how relevant these interpretations of the paper are to the delivery of the LP today and how much they should inform the NICE recommendation process.	benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were base, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the

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					overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Dishonesty Comment: • This section is unrepresentative of the paper as the word 'dishonesty' is mentioned twice in the entire paper and not included in the abstract. It is the last negative aspect reported in the paper but in this table, it has been promoted to the second finding. • The claim 'People criticised the <u>impression</u> that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed <u>when they claimed</u> the treatment had a 100% success rate' is misleading. The quote from one of the two dissatisfied participants is 'I <u>think</u> the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those

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				can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011). - When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach. It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. This section should be revised to express the findings more clearly, for example: 'some felt their practitioner had implied a greater change was possible than was achieved in their case; others reported they were much or very improved. The report notes a survey of LP participants on the LP website found that 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course'	experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. We have no evidence to suggest that 81-86% incorporated people whose statements from the Reme study (included in Evidence review G) supported the committee's concerns about the Lightning Process and if we were to accept this survey data, the percentage of people that still appear to be experiencing concerns is not negligible and would not change decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push

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					through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Review finding: Theory Comment: The positive findings in this section, which reported "Learning the theory behind LP" as a helpful aspect, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. The committee's decision making has been based on the consideration of multiple factors including

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					the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Review finding: Confusing Comment: This theme is at odds with much of the information in the previous theme, 'The Theory', where the educational experience was deemed valuable by many and needs to be reported within that context.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the

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					experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on

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					the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Peer support Comment: The positive findings in this section, which reported one helpful aspect of The Lightning Process was "meeting others with chronic fatigue syndrome", are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation and should be reviewed.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient

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					experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Goal setting Comment: The positive findings in this section are minimised in the narrative sections of the document relating to this study and the LP and as a result, are not reflected in the recommendation. Although there were more helpful aspects reported than less helpful aspects, the review has reported more negative findings which do not reflect the study (Reme et al, 2012). This shows a bias in the review of this qualitative study that needs addressing.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements

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					reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Practice and application Comment: The positive findings in this section, which reported that the "practical assignments" and "practicing the process" were helpful, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE

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					guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Intensity Comment: For context, the LP is often delivered in sessions of 4 hours (Crawley et al., 2018) including breaks as required and is paced and tailored to meet the needs of the individuals attending. This information, available in the published documentation of the process at the time, was unfortunately not reflected in the study. This is compounded by it also not being represented in these documents. This needs to be reviewed and updated.	Thank you for your comment. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol beyond the duration of sessions for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of multiple factors including the different types of evidence available, the trade-off between benefits and harms, economic considerations, resource

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					impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed) and does not eliminate the committee's concerns about the Lightning Process. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Follow up Comment: For context, since the publication of the paper and subsequent audit of practitioners' delivery of the LP, it is standard procedure for all practitioners to deliver a minimum of 3 hours follow up. This renders the relevance of these findings from 2007 to be of doubtful use when making recommendations in 2020. Although this is a matter of public record, it has not been recognised or reported in the evidence document, which as a result needs to be reviewed and updated.	Thank you for your comment. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol beyond the duration of sessions for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of multiple factors including the different types of evidence available, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed) and does not eliminate the committee's concerns about the Lightning Process.

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					In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Effectiveness Comment: The phrasing of this statement, "Some experienced an instant healing; some experienced a gradual improvement that continued after treatment ended and some did not find the treatment helpful." bears little resemblance to the much more positive findings in the study in the original paper they are reported as, "Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved" and "Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better." It is questionable why these positive results have been downplayed in this review. This statement should be rewritten to reflect the study more accurately. Additional note: An error has crept into the reference numbers; 89 references a paper by Taylor, not Reme.	Thank you for your comment. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol beyond the duration of sessions for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of multiple factors including the different types of evidence available, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed) and does not eliminate the committee's concerns about the Lightning Process. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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					Thank you for highlighting this error. All reference numbers have been revisited and corrected where necessary.
Register of Lightning Process Practitioners	Evidence review G	220	Table 78	Secrecy Comment: This statement from 'a (unspecified) few' of the participants, findings which the review concluded there was low confidence in, is of concern to the LP as it is the opposite of the LP's position. Researchers, clinicians and family members have always been welcome to obsegve the LP and there is published information about how the LP works and its entire protocol (Crawley et al., 2018; Parker, 2011, 2013, 2020; Parker et al., 2018). It is standard practice to require any LP participant under 16 to be accompanied by a parent/responsible adult, as evidenced in the RCT (Crawley et al., 2018), and in that study audio recordings were made of the sessions for qualitative analysis. In light of these documented facts, it is clear the LP encourages openness and transparency, and additionally, as the LP is patient-centred there could be no therapeutic value in asking for elements to be kept secret. Additional note: As a result of this study, an audit of how practitioners were delivering the information was undertaken and a specific CPD programme was introduced at the time to ensure this message was communicated even more clearly. In the wording 'The secrecy surrounding the Lightning Process' there seems to be a failure of applying scientific rationale. It is not appropriate to use the experiences reported by '(unspecified) several' of the 9 participants to describe the delivery of the LP in 2007 (when the study was conducted). This should be reflected in this table.	Thank you for your comment. The aim of the qualitative aspect of Evidence review G was to gain insight on people's subjective experience of the interventions received. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', highlight aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process that cannot be discarded. Apart from the findings emerging from the qualitative evidence, the committee have utilised their clinical experience to inform decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual,

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				It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly post-audit. It is irrational, in light of the evidence of the LP's openness and transparency reported above, to continue to perpetuate these claims of secrecy that circulate on the internet, that can be identified throughout this document and has been central to the drafting of these recommendations. This raises serious concerns about the validity of the recommendations which focus so heavily on this point. In light of these issues the recommendations should be reviewed to reflect these facts.	section 9.1 for further details on how recommendations are developed). Confidence in the evidence is considered in decision making, and it was the findings of both positive and negative experiences were rated as low confidence. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were based, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the

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					overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making; and the were additional concerns outlined above that contributed to decision making and the current recommendations. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	250	025 - 036	Dishonesty Comment: • This section is unrepresentative of the paper as the word 'dishonesty' is mentioned twice in the entire paper and not included in the abstract. It is the last negative aspect reported in the paper but in this section, it has been promoted to the second finding.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the

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				• The review concluded there was low confidence in these findings. • The claim 'People criticised the impression that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed when they claimed the treatment had a 100% success rate' is misleading. The quote from one of the two dissatisfied participants is 'I think the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011). • When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach. It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. This section should be revised to express the findings more clearly, for example: 'some felt their practitioner had implied a greater change was possible than was achieved in their case; others reported they were much or very improved. The report notes a survey of LP participants on the LP website found that 81% of the participants reported that they no longer had the	committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements about the dishonesty of the Lightning Process, statements reflecting a pressure to be happy and the encouragement not to talk about the therapy also reflected the experience of some people. Regardless of how many people reported those experiences and irrespectively of whether they have been included in the abstract of the papers they emerged from, those findings have raised the committee's concerns and were considered in decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts' or to be 'true'. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding this intervention. We have no evidence to suggest that 81% of people no longer had issues and even the percentage of people that still appear to be experiencing concerns is not negligible. The committee's decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the

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				issues they came with by Day 3 of the course, and 86% attributed the improvements to the course'	committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	250	009 - 016	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Relationship with the therapist • The section that 'Therapists and staff were mostly described as positive and encouraging. There were different opinions about the therapists.' A positive relationship with a therapist is an essential component of any intervention and in some cases, as with any other intervention, this was not achieved. This does not identify that the intervention causes 'harm' or that that type of relationship experience can be generalised to the LP intervention as a whole. • The review concluded there was low confidence in these findings. • The suggestion that the LP doesn't encourage debate, pressures people 'to be happy all the time and not express any negative feelings' or that it blames them for not getting well is not representative of the LP approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why blame can have no	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy

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				part in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. • It is reported that 7 were much improved and 2 were not. However, it is unclear from the paper to what extent and how many of the participants experienced these specific issues, which, although disappointing to read, are not part of the LP approach. As such, there is a limit to the generalisability of these unquantified reported negative experiences. • When these points are discussed later in the narrative section, the published information about the LP approach has not been included to provide some balance to the reported experiences by these two dissatisfied participants 13 years ago. These points raise questions about how relevant these interpretations of the paper are to the delivery of the LP today, and when combined with the review's low confidence in the paper's findings, how they should not inform the NICE recommendation process.	surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent

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					the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were base, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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Register of Lightning Process Practitioners	Evidence review G	250	007	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Comment: It is questionable why this small scale (n = 9), qualitative study has been given so much prominence in this document when for the following reasons it should be of limited relevance to the discussions on harm and recommendations: • It recruited from a highly selective population, AYME that is a '<u>support</u> organization for young people <u>with</u> CFS.' • Interviews were conducted 13 years ago, and it is questionable how representative it can be of the LP today, particularly as changes in auditing the LP delivery were actioned as a result of its publication. • The diagnostic criteria used (Oxford) meant the participants might not have had post exertional malaise (PEM) as noted by NICE throughout the document. This questions how representative the population might be of those with CFS/ME and therefore, by NICE's own standards, cannot be used as evidence for CFS/ME patients with PEM. • A larger more recent qualitative study (Beasant et al., 2013) was included in the evidence. It found no evidence of negative experience but is less reported on in this document. • A larger scale RCT (n = 100) (Crawley et al., 2018), the accepted method of assessing effects (benefits and harm), found no evidence of serious adverse events related to either treatment arm. It is methodologically surprising that these findings are discarded in favour of the qualitative study (Reme et al., 2012). • The NICE documents note (Evidence G P 321 L 14) that when recurring themes are present across a	Thank you for your comment. Evidence identified for the Lightning Process was limited to the included studies by Reme and Beasant. The committee acknowledged evidence was limited but as with all NICE guidelines, this was not the only source of information that the committee considered. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment and decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance, as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning

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				number of studies (even if of lower quality) they should be given greater weight. This has not happened here, since the positive experiences from the qualitative studies (Beasant et al., 2013; Reme et al., 2012) and the quantitative study (Crawley et al., 2018) have not been given greater weight. This shows a bias and an inconsistency in the review process. • The qualitative study (Reme et al., 2012) was not designed to assess for harm but to provide insights on experiences of the intervention. As a result, it reported on helpful and less helpful aspects of the Lightning Process and none of these reported elements are related to serious adverse events. • In this document, the committee has framed some of the experiences reported in the paper as 'harms', although this is a term completely absent from the study. This has then been used to provide much of the 'evidence' of 'harms' for the recommendations about the LP, but the positive experiences of improvement are not used as evidence of effect. All these points show a concerning inconsistency in process that has resulted in the raising of the prominence of selected less positive findings about the LP from this paper and the downplaying of all the evidence that rebuts them. This biased presentation has then been used to provide the 'evidence' of 'harms' for the recommendations about the LP. We suggest an alternative text that better expresses the evidence presented: that based on the evidence this review reports that the findings from a small scale qualitative study identified positive experiences for most but not all participants. That an RCT identified significantly improved outcomes, when the LP was combined with SMC, and no evidence of serious adverse events related to either treatment arm. Evidence from these studies is too weak to draw any conclusions about this intervention and further research is needed.	Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study that included adolescents taking part in the SMILE trial, was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the qualitative evidence table for this study). Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist' where descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. In addition to those positive experiences, the committee also considered negative experiences emerging from

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					the study. Statements including those reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Such finding supported the committee's concerns about the Lightning Process. As you state the level of confidence in the findings can impact the weight placed on those findings during decision making. The committee did not dismiss or selectively consider any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making and there were additional concerns raised which contributed to the current recommendations. The committee did not consider findings differently based on personal preference, but rather utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform their decision making. They may therefore place greater weight to a lower quality finding when this appears to be in line with what they see in their everyday encounters with people with ME/CFS, as these provide further support about the accuracy with which a finding represents the phenomenon of interest (i.e. the experience of people with ME/CFS). In this case the confidence in both findings illustrating positive and negative experiences of the Lightning Process were assessed to be very low. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, as mentioned earlier the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a

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					recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	251	004 - 010	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Confusing Comment: This theme is at odds with much of the information in the previous theme, 'The Theory', where the educational experience was deemed valuable by many and needs to be reported within that context.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process' that you refer to, Peer support', 'Goal setting', 'Practice and application' highlighting aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements of people who found the theory complicated and difficult to understand also emerged and these were summarised under a separate theme to be taken into consideration along with previous findings as they also provide evidence of peoples' experience of the Lightning Process. Different experiences have been summarised under different review themes to highlight the different experiences emerging from the evidence which may sometimes vary, as was the case here.

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Register of Lightning Process Practitioners	Evidence review G	252	031 - 036	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Effectiveness Comment: The phrasing of this statement: L32-33, “Some experienced an instant healing; some experienced a gradual improvement that continued after treatment ended and some did not find the treatment helpful.”, bears little resemblance to the much more positive findings in the study. It reported, “Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved.” and “Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better.” It is strange that one person's negative experience dominates this paragraph (L 33-36) taking up more space than the 7 of the 9 interviewed, who were ‘very satisfied with the treatment and that they were either much or very much better.” It is concerning why these positive results have been downplayed and the negative responses have been amplified in this review in a way that does not reflect the study. We would suggest this is reviewed to more accurately reflect the paper's findings.	Thank you for your comment. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the ‘Theory behind the Lightning Process’ that you refer to, Peer support', ‘Goal setting', ‘Practice and application' highlighting aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements of people who found the theory complicated and difficult to understand also emerged and these were summarised under a separate theme to be taken into consideration along with previous findings as they also provide evidence of peoples' experience of the Lightning Process. Different experiences have been summarised under different review themes to highlight the different experiences emerging from the evidence which may sometimes vary, as was the case here.
Register of Lightning Process Practitioners	Evidence review G	252	009 - 012	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Intensity This interpretative statement ‘The length of the sessions was thought to be too long and intense' does not reflect the paper's finding ‘Most of them found the format acceptable and helpful, but several comments were raised regarding the intensity of the treatment' and should be changed to reflect the findings more accurately.	Thank you for your comment. As with all qualitative evidence, we carefully consider the information reported in the paper and extracted all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the intervention received and synthesise them into different review findings to capture the multiplicity of experiences people report. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the qualitative evidence table for this study). Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and

				For context, the LP is often delivered in sessions of 4 hours (Crawley et al., 2018) including breaks as required and is paced and tailored to meet the needs of the individuals attending. This information, available in the published documentation of the process at the time, was unfortunately not reflected in the study. This is compounded by it also not being represented in these documents. This needs to be reviewed and updated.	contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist'. In addition to those positive experiences, negative experiences emerging from the study have also been summarised under different themes. That sessions were found to be too long and intense is also reported in the paper and this experience is reflected in the theme of 'Intensity. The fact that other participants found the format of the sessions helpful and acceptable has been considered as well but it does not minimise the experience of those who did not. The multiplicity of themes summarised for the Lightning Process was aimed to capture different experiences. Such statements were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol beyond the duration of sessions for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of multiple factors including the different types of evidence available, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed) and does not eliminate the committee's concerns about the Lightning Process.

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					In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	252	045 - 048	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Secrecy Comment: This statement from 'a (unspecified) few' of the participants, findings which the review concluded there was low confidence in, is of concern to the LP as it is the opposite of the LP's position. Researchers, clinicians and family members have always been welcome to observe the LP and there is published information about how the LP works and its entire protocol (Crawley et al., 2018; Parker, 2011, 2013, 2020; Parker et al., 2018). It is standard practice to require any LP participant under 16 to be accompanied by a parent/responsible adult, as evidenced in the RCT (Crawley et al., 2018), and in that study audio recordings were made of the sessions for qualitative analysis. In light of these documented facts, it is clear the LP encourages openness and transparency, and additionally, as the LP is patient-centred there could be no therapeutic value in asking for elements to be kept secret. Additional note: As a result of this study, an audit of how practitioners were delivering the information was undertaken and a specific CPD programme was introduced at the time to ensure this message was communicated even more clearly.	Thank you for your comment and information. The aim of the qualitative aspect of Evidence review G was to gain insight on people's subjective experience of the interventions received. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', highlight aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process that cannot be discarded. Apart from the findings emerging from the qualitative evidence, the committee have utilised their clinical experience to inform

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				In the wording 'The secrecy surrounding the Lightning Process' there seems to be a failure of applying scientific rationale. It is not appropriate to use the experiences reported by '(unspecified) several' of the 9 participants to describe the delivery of the LP in 2007 (when the study was conducted). This should be reflected in this section. It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly post-audit. It is irrational, in light of the evidence of the LP's openness and transparency reported above, to continue to perpetuate these claims of secrecy that circulate on the internet, that can be identified throughout this document and has been central to the drafting of these recommendations. This raises serious concerns about the validity of the recommendations which focus so heavily on this point. In light of these issues the recommendations should be reviewed to reflect these facts.	decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Evidence confidence is also considered in decision making, and it was findings of both positive and negative experiences that were of low confidence. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were based, was downgraded for moderate concerns

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					over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making; and the were additional concerns outlined above that contributed to decision making and the current recommendations. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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Register of Lightning Process Practitioners	Evidence review G	252	021 - 022	2.1.5.11 Narrative summary of review findings for children/young people (severity mixed or unclear) who have had the Lightning Process Review finding: Follow up Comment: For context, since the publication of the paper and subsequent audit of practitioners' delivery of the LP, it is standard procedure for all practitioners to deliver a minimum of 3 hours follow up. This renders the relevance of these findings from 2007 to be of doubtful use when making recommendations in 2020. Although this is a matter of public record, it has not been recognised or reported in the evidence document, which as a result needs to be reviewed and updated.	Thank you for your comment. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol beyond the duration of sessions for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of multiple factors including the different types of evidence available, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed) and does not eliminate the committee's concerns about the Lightning Process. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	253	009 - 048	2.1.5.12 Narrative summary of review findings for children/young people (mild/moderate) who have had the Lightning process Comment: This qualitative study (Beasant et al., 2013)) is more recent and had a larger number of participants (N = 25) than the Reme study (2012) (Evidence G P 220 Table 78). Participants were asked	Thank you for your comment. The aim of the Beasant 2014 study that included adolescents taking part in the SMILE trial, was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings appeared more relevant to the specialist service in general rather

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				about their experiences of the interventions which included the LP. Questions asked included: Tell me about the intervention you received? Prompts: What happened? What was good/bad? What would you change? Venue? Structure of sessions? Language used? Was it as expected? No negative responses or harms were reported in the paper, and although this would seem important to note in comparison to the Reme study (2012) this is not presented in the review. This appears to be an inconsistency in the NICE documentation and has affected the recommendation process. This information needs to be reflected in the recommendation.	than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee acknowledge that it is difficult to quantify harms from qualitative studies. The aim of the qualitative review was to highlight peoples' subjective experiences of interventions including the Lightning Process. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the qualitative evidence table for this study). Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist' where descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. In addition to those positive experiences, the committee also considered negative experiences emerging from the study. Statements including those reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Such finding supported the committee's concerns about the Lightning Process.

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					The committee also acknowledged evidence was limited but as with all NICE guidelines, this was not the only source of information that the committee considered. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment and decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	301	005	2.1.6 Qualitative evidence summary Table 91: Summary of evidence: The Lightning Process General Comments: This table interprets the findings of a qualitative study (Reme et al., 2012), which is used as the primary evidence about the LP throughout the rest of the document. There are issues with this	Thank you for your comment. Evidence identified for the Lightning Process was limited to the included studies by Reme and Beasant. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the

				study's relevance and how it has been reported here and elsewhere in the document. Of particular concern is a downplaying in this review of the key finding that: • Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved. • Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better. • That 7 of the 9 no longer met the criteria for CFS/ME after attending the Lightning Process. There is also a selective highlighting of less positive experiences that is unrepresentative of the paper and a series of misinterpretations of the paper's findings. These concerning issues of bias, detailed in the comments that follow, make the reliance on this interpretation of paper as the primary source of evidence, and a basis for any recommendation, unsound. We would suggest that this table be rewritten in a way which reflects the paper's findings more accurately. Detailed comments: Relationship with the therapist Comment: • The table notes that 'Therapists and staff were mostly described as positive and encouraging. There were different opinions about the therapists.' A positive relationship with a therapist is an essential component of any intervention and in some cases, as with any other intervention, this was not achieved. This does not identify that the intervention causes 'harm' or that that type of relationship experience can be generalised to the LP intervention as a whole.	interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered As you note the themes, 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlight aspects of the interventions that people had found helpful and the 'Relationship with the therapist' where as you state descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Sessions were reported to be too long and intense and this experience is reflected in the theme of 'Intensity. The fact that other participants found the format of the sessions helpful and acceptable has been considered as well but it does not minimise the experience of those who did not. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical considerations surrounding the Lightning Process. We have no evidence to suggest that 81% of people no longer had issues and even then the percentage of people that still appear to be experiencing concerns is not negligible. The committee's decision making has been based on the consideration of multiple factors. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact,

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				• The suggestion that the LP doesn't encourage debate, pressures people 'to be happy all the time and not express any negative feelings' or that it blames them for not getting well is not representative of the LP approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why blame can have no part in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. • It is reported that 7 were much improved and 2 were not. However, it is unclear from the paper to what extent and how many of the participants experienced these specific issues, which, although disappointing to read, are not part of the LP approach. As such, there is a limit to the generalisability of these unquantified reported negative experiences. • When these points are discussed later in the narrative section, the published information about the LP approach has not been included to provide some balance to the reported experiences by these two dissatisfied participants 13 years ago. This raises questions about how relevant these interpretations of the paper are to the delivery of the LP today and how much they should inform the NICE recommendation process. Dishonesty Comment: • This section is unrepresentative of the paper as the word 'dishonesty' is mentioned twice in the entire paper and not included in the abstract. It is the last negative	clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were base, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to

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				aspect reported in the paper but in this table, it has been promoted to the second finding. - The claim 'People criticised the <u>impression</u> that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed <u>when they claimed</u> the treatment had a 100% success rate' is misleading. The quote from one of the two dissatisfied participants is 'I <u>think</u> the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011). - When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach. It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. This section should be revised to express the findings more clearly, for example: 'some felt their practitioner had implied a greater change was possible than was achieved in their case; others reported they were much or very improved. The report notes a survey of LP participants on the LP website found that 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course'	very low. The Beasant 2014 study also contributing to findings for the Lightning Process, included adolescents taking part in the SMILE trial and was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making; and the were additional concerns outlined above that contributed to decision making and the current recommendations. After reviewing the evidence including both positive and negative experiences of the Lightning Process, the committee's concerns associated with the lack of transparency about aspects of the research and the treatment protocol outlined above go beyond the duration of sessions for the Lightning Process. The information you kindly provide is not sufficient to change decision making that has been based on the consideration of the multiple factors outlined above. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				Theory Comment: The positive comments in this section, which reported "Learning the theory behind LP" as a helpful aspect, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation. Confusing Comment: This theme is at odds with much of the information in the previous theme, 'The Theory', where the educational experience was deemed valuable by many and needs to be reported within that context. Peer support Comment: The positive comments in this section, which reported one helpful aspect of The Lightning Process was "meeting others with chronic fatigue syndrome", are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation and should be reviewed. Goal setting Comment: The positive comments in this section are minimised in the narrative sections of the document relating to this study and the LP and as a result, are not reflected in the recommendation. Although there were more helpful aspects reported than less helpful aspects, the review has reported more negative findings which do not reflect the study (Reme et al, 2012). This shows a bias in the review of this qualitative study that needs addressing.	

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				Practice and application Comment: The positive comments in this section, which reported that the "practical assignments" and "practicing the process" were helpful, are minimised in the narrative sections of the document relating to this study and the LP. This suggests a bias and has resulted in these positive aspects not being reflected in the recommendation. Intensity Comment: This interpretative statement 'The length of the sessions was thought to be too long and intense' does not reflect the paper's finding 'Most of them found the format acceptable and helpful, but several comments were raised regarding the intensity of the treatment' and should be changed to reflect the findings more accurately. For context, the LP is often delivered in sessions of 4 hours (Crawley et al., 2018) including breaks as required and is paced and tailored to meet the needs of the individuals attending. This information, available in the published documentation of the process at the time, was unfortunately not reflected in the study. This is compounded by it also not being represented in these documents. This needs to be reviewed and updated. Follow up Comment: For context, since the publication of the paper and subsequent audit of practitioners' delivery of the LP, it is standard procedure for all practitioners to deliver a minimum of 3 hours follow up. This renders the relevance of these findings from 2007 to be of doubtful use when making recommendations in 2020. Although this is a matter of public record, it has not been recognised or reported in the evidence document, which as a result needs to be reviewed and updated.	

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				Effectiveness Comment: The phrasing of this statement, "Some experienced an instant healing; some experienced a gradual improvement that continued after treatment ended and some did not find the treatment helpful." bears little resemblance to the much more positive findings in the study in the original paper they are reported as, "Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved" and "Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better." It is questionable why these positive results have been downplayed in this review. This statement should be rewritten to reflect the study more accurately. Secrecy Comment: This statement from 'a (unspecified) few' of the participants is of concern to the LP as it is the opposite of the LP's position. Researchers, clinicians and family members have always been welcome to observe the LP and there is published information about how the LP works and its entire protocol (Crawley et al., 2018; Parker, 2011, 2013, 2020; Parker et al., 2018). It is standard practice to require any LP participant under 16 to be accompanied by a parent/responsible adult, as evidenced in the RCT (Crawley et al., 2018), and in that study audio recordings were made of the sessions for qualitative analysis. In light of these documented facts, it is clear the LP encourages openness and transparency, and additionally, as the LP is patient-centred there could be no therapeutic value in asking for elements to be kept secret.	

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				Additional note: As a result of this study, an audit of how practitioners were delivering the information was undertaken and a specific CPD programme was introduced at the time to ensure this message was communicated even more clearly. In the wording 'The secrecy surrounding the Lightning Process' there seems to be a failure of applying scientific rationale. It is not appropriate to use the experiences reported by '(unspecified) several' of the 9 participants to describe the delivery of the LP in 2007 (when the study was conducted). This should be reflected in this table. It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly post-audit. It is irrational, in light of the evidence of the LP's openness and transparency reported above, to continue to perpetuate these claims of secrecy that circulate on the internet, that can be identified throughout this document and has been central to the drafting of these recommendations. This raises serious concerns about the validity of the recommendations which focus so heavily on this point.	
Register of Lightning Process Practitioners	Evidence review G	306	005	2.1.6 Qualitative evidence summary Table 92: Summary of evidence: The Lightning Process (mild/moderate severity) This qualitative study (Beasant et al., 2013)) is more recent and had a larger number of participants (N = 25) than the Reme study (2012) (Evidence G P 220 Table 78). Participants were asked about their experiences of the interventions which included the LP. Questions asked included: Tell me about the intervention you received? Prompts: What happened? What was good/bad? What would you change? Venue? Structure of sessions? Language used? Was it as expected?	Thank you for your comment. The aim of the Beasant 2014 study that included adolescents taking part in the SMILE trial, was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings appeared more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. The committee acknowledge that it is difficult to quantify harms from qualitative studies. The aim of the qualitative review was to highlight peoples' subjective experiences of interventions including the Lightning Process. When reviewing qualitative evidence, we carefully consider the information reported in each

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				No negative responses or harms were reported in the paper, and although this would seem important to note in comparison to the Reme study (2012) this is not presented in the review. This appears to be an inconsistency in the NICE documentation and has affected the recommendation process. This information needs to be reflected in the recommendation.	paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. All the information extracted from the Reme study can be found in Appendix D in Evidence review H (in the qualitative evidence table for this study). Positive accounts of the Lightning Process emerging from the Reme study have been synthesised and contribute to various review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'Peer support', 'Goal setting', 'Practice and application' which all highlight aspects of the interventions that people had found helpful, but also under 'Relationship with the therapist' where descriptions of staff as positive and encouraging have been included together with accounts of people who had a less positive experience. In addition to those positive experiences, the committee also considered negative experiences emerging from the study. Statements including those reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process. Such finding supported the committee's concerns about the Lightning Process. The committee also acknowledged evidence was limited but as with all NICE guidelines, this was not the only source of information that the committee considered. Apart from the findings emerging from the qualitative evidence, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment and decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between

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					benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.
Register of Lightning Process Practitioners	Evidence review G	321	014	3.2.2 The quality of the evidence - qualitative review of experiences of interventions Comment This statement evidences impartiality: *In general, the committee placed greater weight on moderate confidence findings than low* *15 and very low confidence findings during discussion of the evidence, although they* *16 acknowledged that some lower confidence findings <u>reflected their own experience</u> and* *17 should not be disregarded.* There is a lack of scientific rigour in allowing the experiences of the committee members to dictate how the published evidence is interpreted or valued. This is particularly concerning when the	Thank you for your comment. The level of confidence given to each finding is important as it reflects confidence in the extent to which findings are an accurate representation of the phenomenon of interest and in this case of people's experience of interventions including the Lightning Process. When a finding is of low or very low confidence, it means that concerns about the accuracy with which a review finding reflects the experience of people with ME/CFS are more serious and placing greater weight on findings with a higher confidence rating helps ensure the quality standard of the guideline. Nevertheless, regardless of the level of confidence, the committee did not disregard any findings and the level of confidence in only one of the elements considered by the committee during decision making along with factors including

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				committee is unrepresentative of patients who have recovered from CFS/ME and includes those who have an identified lack of impartiality towards the LP (see evidence in comments 32, 35-37). It continues, evidencing an inconsistency in process: *The committee also acknowledged that some <u>common themes</u> 18 were identified across <u>multiple review strata</u> and that lower confidence findings contributing 19 to these themes could be interpreted with <u>higher confidence</u> when considered across 20 studies.* The Reme study (2012) reported far more positive experiences (7) than negative (2), as did the Beasant study (2013) and the SMILE RCT (2018) found significant effects when the LP was combined with SMC and no serious adverse events. This recurring theme supports studies with 'lower quality evidence' and the committee should therefore be, based on the evidence, learning towards cautious interest in further research rather than stating 'do not recommend the LP'. What is the rationale for not applying this theme identification, as identified in this statement, across these three studies?	the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee does not consider findings differently based on personal preference, but rather utilise their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform their decision making. They may therefore place greater weight to a lower quality finding when this appears to be in line with what they see in their everyday encounters with people with ME/CFS, as these provide further support about the accuracy with which a finding represents the phenomenon of interest (i.e. the experience of people with ME/CFS). In regard to the Lightning Process, the committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. As noted The evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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Register of Lightning Process Practitioners	Evidence review G	329	033 - 038	The committee´s discussion and interpretation of the evidence 3.3 Benefits and harms Other psychological/behavioural interventions Review of clinical and cost effectiveness Adults Comment: The results of this RCT (Crawley et al., 2018) have been minimised in this document. 'Data from 81 participants were analysed at 6 months. Physical function (SF-36-PFS) was better in those allocated SMC+LP (adjusted difference in means 12.5 [95% CI 4.5 to 20.5], p=0.003) and this improved further at 12 months (15.1 [95% CI 5.8 to 24.4], p=0.002). At 6 months, fatigue and anxiety were reduced and at 12 months, fatigue, anxiety, depression and school attendance had improved in the SMC+LP arm. Results were similar following multiple imputation. SMC+LP was more cost-effective in the multiple imputation data set (difference in means in net monetary benefit at 12 months £1474 [95% CI £111 to £2836], p=0.03) but not for complete cases.' 'Participants in the SMC+LP arm maintained, or increased improvements compared with SMC alone at 12 months and this was true for both the ITT and the CACE analyses. This is in contrast to previous trials investigating internet-based CBT where the treatment effects were sustained but the difference between the two trial arms was reduced at 12 months compared with 3 months and family-focused CBT versus psychoeducation where treatment differences at 3 months were not maintained at 6 or 12 months.'	Thank you for your comment. The committee acknowledged that evidence from one RCT on the Lightning Process (SMILE) showed some evidence of benefit of the Lightning Process. However, this was not the only evidence the committee considered when making their recommendations. When developing this guideline the committee considered a wide range of evidence, including that from published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature, including children and young people. See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed. The committee acknowledged the evidence of benefit seen in the SMILE trial, however they had several concerns. The committee were particularly concerned by the lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. Additionally. they agreed that evidence for the Lightning Process was limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on

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				Conclusion: The LP is effective and is probably cost-effective when provided in addition to SMC for mild/moderately affected adolescents with CFS/ME. Additionally, an important statement is not reported here – that no serious adverse events were reported as a result of either arm of the trial. As the NICE recommendations should reflect the evidence base, it is difficult to see any logical reason why these findings, which are so central to that process, have been ignored. This omission shows a bias in the reporting of these studies and an inconsistency that has informed the development of the recommendations. This section should be reviewed to reflect these findings.	the principles of energy management and this therapy is at odds with these principles. With regards to serious adverse events, thank you for pointing this out. This outcome has now been added to the review.
Register of Lightning Process Practitioners	Evidence review G	332	001 - 013	The committee´s discussion and interpretation of the evidence 3.3 Benefits and harm Overall – other psychological/behavioural interventions Comments: The study's findings are misrepresented throughout this section. L3 'overall effectiveness was mixed' 'Mixed' is an inaccurate reporting of the actual quote from the paper's abstract: 'Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved.' 'L4 some harms were reported' This is misleading and inaccurate. The paper does not mention 'harm' at any point. This is a frame the committee has chosen to put around these findings and is not supported by the study. Accepted methods for assessing harm are RCTs rather than qualitative studies of small numbers of participants.	Thank you for your comment. The statement about 'overall effectiveness' has been amended and the word 'harm' has been removed to reflect this referred to both positive and negative experiences of the Lightning Process emerging from the qualitative evidence. The aim of the qualitative aspect of Evidence review G was to gain insight on people's subjective experience of the interventions received. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process have been synthesised and contribute to different review findings that the committee has considered, such as the theme titled the 'Theory behind the Lightning Process', 'goal setting' which highlight aspects of the interventions that people had found helpful. However, this was not representative of the experience of all people included in the evidence for the Lightning Process.

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				The RCT (Crawley et al., 2018) found no evidence of serious adverse events. The Beasant qualitative study (2013) also reported no negative experiences. The instruction to consider themes present across these papers (Evidence G P 321 L 14), i.e. 'no evidence of harm' has been ignored in this case. The responses to the questions asked by researchers about the less positive aspects of their experience in this study (Reme et al., 2012) provided a valuable opportunity for reflection. As a result of these issues being raised by the study, an audit of how practitioners were delivering the materials, information and managing the seminars was undertaken. A specific CPD programme was subsequently introduced to ensure these messages were communicated even more clearly and the high standards expected of LP practitioners were being universally upheld. These important documented responses and procedures (Parker, 2020; Parker et al., 2018) are not reflected in the NICE review. This lack of reference to the facts concerning openness, documentation of the intervention and the patient-centred approach of the LP is compounded by the inaccurate way that the statements of negative experience (itemised below) have been reported and is of great concern. L4 'confusing'. This theme is at odds with much of the information in the previous theme, 'The Theory', where the educational experience was deemed valuable by many as evidenced by the report 'The explaining of the process, the background information definitely helped because it helps you realize how the process works'. This theme should be viewed within that context, something that is absent from this review. L5 'intensity'. The study (Reme et al., 2012) reports that 'Most of them found the format acceptable and helpful,' and this is not	Negative experiences including statements reflecting dissatisfaction, a lack of improvement, a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Sessions were reported to be too long and intense and this experience is reflected in the theme of 'Intensity. The fact that other participants found the format of the sessions helpful and acceptable has been considered as well but it does not minimise the experience of those who did not. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process that cannot be discarded. We have no evidence to suggest that 81% of people no longer had issues, and even then the percentage of people that still appear to be experiencing concerns is not negligible and would not change decision making that has been based on the consideration of multiple factors. The Beasant study, including adolescents taking part in the SMILE trial, also contributed to findings for the Lightning Process. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. Also, after considering stakeholder comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional

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				reflected in this review, which misreports it as 'The length of the sessions was thought to be too long and intense'. For context, the LP is often delivered in sessions of 4 hours (Crawley et al., 2018) including breaks as required and is paced and tailored to meet the needs of the individuals attending. This information, available in the published documentation of the process at the time, was unfortunately not reflected in the study. This is compounded by it also not being represented in these documents. L5 Alleged 'secrecy'. This statement from 'a (unspecified) few' of the participants is of concern to the LP as it is the opposite of the LP's position. Researchers, clinicians and family members have always been welcome to observe the LP and there is published information about how the LP works and its entire protocol (Crawley et al., 2018; Parker, 2011, 2013, 2020; Parker et al., 2018). It is standard practice to require any LP participant under 16 to be accompanied by a parent/responsible adult, as evidenced in the RCT (Crawley et al., 2018), and in that study audio recordings were made of the sessions for qualitative analysis. In light of these documented facts, it is clear the LP encourages openness and transparency, and additionally, as the LP is patient-centred there could be no therapeutic value in asking for elements to be kept secret. This issue was a central point addressed by the practitioners' audit. A CPD programme was introduced at the time to ensure this message was communicated even more clearly. This is not reflected in the review. There seems to be a failure of applying scientific rationale with this statement. It is not appropriate to use the experiences reported by '(unspecified) several' of the 9 participants to describe the delivery of the LP in 2007 (when the study was conducted). It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly post-audit. It is irrational, in light of the evidence	concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance as the committee agreed that evidence based on populations not experiencing PEM, may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After revisiting all the studies, the Reme study upon which the majority of findings for the Lightning Process were based, was downgraded for moderate concerns over applicability as, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making. Quantitative evidence was limited to one RCT and the quality of the evidence also ranged from very low to low. Apart from the findings emerging from both the qualitative and the quantitative evidence, the committee utilised their clinical experience to inform decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the

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				of the LP's openness and transparency reported above, to continue to perpetuate these claims of secrecy that circulate on the internet, that can be identified throughout this document and has been central to the drafting of these recommendations. This raises serious concerns about the validity of the recommendations which focus so heavily on this point. L5-6 'Pressure, blame, dishonesty'. The study reports that 'The therapists and staff were mostly described as positive and encouraging.' A positive relationship with a therapist is an essential component of any intervention and in some cases, as with any other intervention, this was not achieved. This does not identify that the intervention causes 'harm' or that that type of relationship experience can be generalised to the LP intervention as a whole. The suggestion that the LP doesn't encourage debate, pressures people 'to be happy all the time and not express any negative feelings' or that it blames them for not getting well is not representative of the LP approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why blame can have no part in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. This comment about dishonesty is unrepresentative of the paper as the word is mentioned twice in the entire paper and not included in the abstract. This is based on the earlier misinterpretation of the paper in these documents, with the claim 'People criticised the impression that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed when they claimed the treatment had a	committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				100% success rate'. This statement is misleading and inaccurate. The quote from one of the two dissatisfied participants is 'I think the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011).' When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach. It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. L5-6 'some practitioners. There seems to be a failure of applying scientific rationale in using this statement to support the NICE draft recommendation. It cannot be appropriate to use the experiences reported by only 'some' of the 9 participants about 'some' of the practitioners, to describe the delivery of the LP as a whole in 2007. It is also not logically valid to use these selective reports to assume this reflects the delivery of the LP 13 years later, particularly in light of the audit and CPD programmes that followed this paper's publication and when more recent studies with more participants found positive experiences, no evidence of adverse events and improved outcomes (from the addition of the intervention to SMC) (Crawley et al., 2018). This raises serious	

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				concerns about the validity of the recommendations which focus so heavily on this point. The presence of personal opinions affecting the report can also be seen in this statement: 'L7 The committee were aware that some children had been told not to discuss the therapy with their carer or parents." As the published evidence (Beasant et al., 2013; Crawley et al., 2018; Parker, 2013, 2020; Parker et al., 2018, 2018), the fact that parents accompany all children under 16 and that audio recordings of the intervention occur during research does not support this, this 'awareness' must be based on anecdotes and opinion and identifies a concerning lack of impartiality in the committee. Unaware of the error underpinning their assumptions about the intervention the committee 'L8 agreed this was an inappropriate and harmful message to give to children and young people.' Although it would be harmful to give this message to young people it is not what the LP does, as supported by the published evidence. In this flawed statement, the committee shows that they have not read the evidence and have simply assumed this incorrect opinion was accurate. 'L9 The committee considered these findings were applicable to adults as well as children and young people and therefore, The above statement is inaccurate and not supported by the evidence base as already mentioned. It also identifies a further failure of scientific rationale, as there is no evidence that supports generalising these qualitative study findings from one age group to another. 'L10 the committee decided to make a recommendation not to offer therapies derived from osteopathy, life coaching and neuro-	

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				linguistic programming (for example the Lightning Process) to treat or cure ME/CFS.' This decision to make a recommendation not to offer the LP is clearly made on perspectives that lack impartiality and are based on an unsound selective exclusion and interpretation of the evidence. We request that there is a truly independent review and interpretation of the evidence and a redrafting of this section. We suggest that based on the presented evidence base it would be reasonable to treat the LP's evidence in a similar way to that of mindfulness (which has a similar level of evidence to the LP presented in this document) or any of the complementary therapies the report mentions, which have less evidence, and report that currently there is not enough evidence to make any recommendations. NICE guidelines have a robust reputation for being driven by the evidence. This un-impartial draft has failed to uphold those important standards and if unamended raises serious concerns about the validity of recommendations from this usually impartial and research-driven organisation.	
Register of Lightning Process Practitioners	Evidence review G	342	027 - 044	The committee´s discussion and interpretation of the evidence Overall summary of non-pharmacological interventions for ME/CFS Comment: In L34-35 the committee states they 'agree there is no current non-pharmacological treatment or cure for CFS.' This statement raises questions. The concerns about evidence interpretation have already been raised in these comments, but here the	Thank you for your comment. Thank you for your comment. Please note the word treatment has been removed from the wording 'treatment or cure' throughout the guideline to avoid any misinterpretation with the availability of treatments for the symptom management of people with ME/CFS. We appreciate your concern regarding representativeness and we agree on the importance of carefully considering all the information available on the populations included in the evidence in order to identify any factors potentially limiting representativeness and account for them in the assessment of confidence in the findings which is taken into

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				experiences of those with ME/CFS have been included in the decision. It is excellent that patients are being consulted, but questionable how representative these patients are of the whole population of those with ME/CFS. It appears that no groups of those who had been diagnosed and recovered have been included in the capturing of experiences and perspectives. Without this full representation, this statement cannot be supported. L37 The statement, which at least partially is directed at the LP that 'The committee were <u>aware</u> of interventions that are promoted as cures' relates to the committee's suggestions of unsubstantiated promises of cure that appear to be derived from previously held opinions, not supported by the evidence base and the misreporting of the Reme paper(2012) in the evidence document. The interpretative statement 'People criticised the impression that staff gave about the Lightning Process always involving a quick recovery and the dishonesty staff showed when they claimed the treatment had a 100% success rate' is misleading and inaccurate. The quote from one of the two dissatisfied participants is 'I think the people that run it say they have 100% success rate, but obviously, that is not true'. The paper, however, evidences that this 'impression' the respondent had is not supported by the facts. This can be seen in the section reporting that 'although surveys of people attending the programme in Norway and UK show some promise; 81% of the participants reported that they no longer had the issues they came with by Day 3 of the course, and 86% attributed the improvements to the course (Parker, 2011).' When this impression of the participant and evidence in the papers' report of transparency of success rates are considered it cannot be inferred that the staff were dishonest, or that the LP as a whole is a dishonest approach.	account in decision making. This approach has been followed across evidence reviews and for all evidence considered within the present guideline. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. Apart from the different types of evidence considered in the present guideline, the committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making. For the qualitative aspect of the interventions review (Evidence review G) the committee were interested in people's subjective experience of the interventions received rather than what can be stated to be 'the facts'. These statements have therefore been taken into consideration as they are evidence of peoples' experience of the Lightning Process. We have no evidence to suggest that 81% of people no longer had issues , and even then the percentage of people that still appear to be experiencing concerns is not negligible and would not change decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation. Also, after considering the stakeholder

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				It is irrational that this statement gets such high prominence in the NICE documents in the absence of any substantive evidence to support its inclusion as a fact, especially when the evidence presented in the paper confirms that this is not a claim the LP makes. 'L38 and there is often a financial cost when these are pursued.' This is a strange comment to make. Almost all interventions come at a cost, those delivered by the NHS are paid for indirectly but are not cost free. There is also a circular argument here: without NICE approval for an intervention, its delivery by the NHS is unlikely. Patients wanting to access this intervention will therefore have to bear the costs, which is seen, according to this statement, as a reason for NICE to judge it in a negative way. There also seems to be the suggestion of a negative correlation between direct cost and outcomes, which is unsupported by any evidenced presented here. We recommend this section be removed. L 39 'To address this the committee made a recommendation to raise awareness that there is no current non-pharmacological treatment of cure for people with ME/CFS. In addition, the committee made 'do not' offer recommendations for CBT, therapy based on physical activity or exercise therapies derived from osteopathy, life-coaching and neuro-linguistic programming (for example the Lightning Process), and supplements to treat or cure ME/CFS.' This statement does not reflect the evidence. • The LP is not a 'physical activity or exercise' therapy. The evidence base expresses (Parker, 2013, 2020; Parker et al., 2018; Reme et al., 2012) this clearly and the NICE documents are inconsistent, often categorising it as a 'psychological support' approach.	comments the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of the findings they contribute to and in turn on the overall assessment of confidence in the findings. As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. After revisiting all the studies, the Reme study was downgraded for moderate concerns over applicability as, as you state, study participants were reported to meet the Oxford (Sharpe 1991) criteria prior to undergoing the Lightning Process, where PEM is not a compulsory feature for the diagnosis of ME/CFS and there were no further details on the population to suggest they experienced PEM. This resulted in the overall confidence in the findings being downgraded from low to very low. The committee did not dismiss any findings but the level confidence of the findings, which was compromised in the case of the Lightning Process, impacts the weight placed on those findings during decision making. The Beasant 2014 study that included adolescents taking part in the SMILE trial, was not downgraded for concerns over relevance of the population, since the NICE 2007 criteria that include PEM were used for diagnosis in the SMILE trial. However, the aim of the study was to understand the experiences of accessing and using a specialist service (some had not yet used the service) and it was unclear to which intervention arm the findings related to and findings seemed to be more relevant to the specialist service in general rather than the Lightning Process . This limited the extent to which conclusions about the Lightning Process could be drawn from this study. In addition the committee discussed concerns that the Lightning Process encourages people with ME/CFS to ignore and 'push

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				• As the participants were included on the basis of the Oxford criteria for CFS/ME, according to NICE documentation, they might therefore not be representative of patients with CFS/ME. • The evidence from the Reme study (2012), much quoted here has been inaccurately interpreted and framed as evidence of 'harm', although this is a term completely absent from the study. The paper did report seven of the nine participants 'were much improved.' and 'Eight of nine participants met UK criteria (Sharpe et al., 1991) for CFS prior to undergoing the Lightning Process. It is difficult to understand this inconsistency in ignoring positive results of recovery and amplifying negative experiences from the same paper. • With the audit and other actions the LP Register took in response to this study to address the issues it raised these selected findings are not representative of the LP in 2020. • The dismissal of the theme of improved outcomes across the Reme study (2012) and SMILE RCT (Crawley et al., 2018) and the reported absence of serious adverse events. • To make recommendations based on a 13 year old qualitative study is unscientific, particularly when action has been taken to address the issues raised and when more recent studies (Beasant et al., 2013; Crawley et al., 2018) with more participants found positive experiences, no evidence of adverse events and improved outcomes (from the addition of the intervention). A more reasonable conclusion to draw from the data would be 'our interpretation of the current evidence does not allow us to make any recommendations about the LP' and a call for more	through' their symptoms and this could potentially cause harm. The committee noted they had made clear recommendations on the principles of energy management and this therapy is at odds with these principles.

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				research based on the positive findings reported. The comments throughout this response form on this section highlight the failure in process and a lack of impartiality that is a theme running through much of the production of these guidelines.	
Register of Lightning Process Practitioners	Evidence review G	344	004 - 011	The committee´s discussion and interpretation of the evidence 3.4 Cost effectiveness and resource use Other psychological/behavioural interventions Comment: 4 One study evaluated the Lightning Process compared with specialist medical care for young 5 people. The study found a substantial improvement in QALYs, which cost only £3,400 per 6 QALY gained. However, in the evidence on people's experiences (noted above) some harms 7 were reported around the confusing nature of the educational component, the intensity of the 8 sessions, the secrecy surrounding the therapy, the approach of some therapists which led to 9 feelings of pressure and blame and dishonesty about the success rate. These concerns are 10 not likely to be fully captured in the QALYs. Therefore, the committee decided to make a 11 recommendation against the use of the Lightning Process. This section concerns the economic value of the intervention. However, the selective reporting and misleading framing and interpretation of the Reme qualitative study (2012) has again been imported into this section. The same comments (5-18) concerning a lack of impartiality that has affected the reporting of the original paper also apply to this statement.	Thank you. The committee noted the positive as well as negative outcomes reported in the trial and qualitative study. However, they remained concerned about the lack of transparency and secrecy, which is of particular concern when it comes to children, young people and other vulnerable groups. The committee agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated. For this reason, the committee decided that the Lightning Process should not be recommended despite the positive cost-effectiveness evidence. .
Register of Lightning	General	General	General	Conflict of interest/Lack of impartiality - Charles Shepherd	Thank you for your comment.

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Process Practitioners				Charles Shepherd has a well-recorded history of animosity towards the LP. Unfortunately, this lack of impartiality, as evidenced below, makes him unsuitable to contribute to the discussions. Evidence: a) In an interview in 2014: Q: What is your opinion of something like the Lightening Process? *A: I have been very critical of the Lightning Process* (https://www.massmecfs.org/images/pdf/Web_seminar_35-42_and_chats.pdf) b) In The Times 2011: *'Shepherd describes it as 'a 3 day brain-washing session'* ' (https://www.thetimes.co.uk/article/me-lightning-cure-or-a-flash-in-the-pan-87cq3kktkwn). This description is not backed up by the published information detailing the intervention. It identifies his lack of awareness of the intervention, as he has no direct experience of it, and a reliance on selective opinions. c) In 2017, although there is no evidence to support his assertion, Charles Shepherd dismissed positive anecdotes of recovery of those using the LP as not having real ME. *"It may well be that there are some people with a general fatigue state resulting from stress, emotional or psychological problems who could benefit from a 'mind over matter' retraining approach such as this. Such fatigue states are a separate entity and not to be confused with ME/CFS."* (https://meassociation.org.uk/2017/09/me-association-statement-lightning-process-and-smile-trial-in-young-people-with-mecfs-19-september-2017/). This opinion that anyone who has recovered from this serious illness using this method could not have really had it shows a failure of scientific rationale and a concerning disrespect for those with this illness. Instead, he promoted negative anecdotes "Patient evidence, gathered from our members over many years, indicates that	The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared. The Register of interests on the NICE website sets out the declared interests of Dr Charles Shepard and the actions taken to address them. See the Policy on declaring and managing interests for NICE advisory committees for more information on how interests are managed(https://www.nice.org.uk/ Media/Default/About/Who-we-are/Policies-and-procedures/ declaration-of-interests-policy.pdf).

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				some people who have gone through the LP try to make rapid and unrealistic improvements in their physical and mental activity levels. However, this is followed by a relapse or significant worsening of symptoms." This shows his selective confirmation bias for promoting information that matches his opinion. The peer-reviewed papers and books on the intervention identify how his description of it is at odds with the published evidence. (https://meassociation.org.uk/2017/09/me-association-statement-lightning-process-and-smile-trial-in-young-people-with-mecfs-19-september-2017/) d) He has an unscientific anti-research bias against the LP: In 2011, in the absence of an evidence base to support his claim, 'Dr Shepherd backed the ethical challenge (opposing the RCT), which included the claim that it was unethical to carry out the trial in children, made by the ME Association and the Young ME Sufferers Trust. After re-opening its ethical review and reconsidering the evidence in the light of the challenge, the regional ethics committee of the NHS reiterated its support for the trial.' https://www.bmj.com/bmj/section-(pdf/187262?path=/bmj/342/7812/Feature.full.pdf) It can be seen from this that Charles Shepherd holds personal opinions based on his selective interpretation of second-hand reports of the LP and the lack of impartiality evidenced here should exclude him from the committee.	
Register of Lightning Process Practitioners	General	General	General	Conflict of interest/Lack of impartiality - Adam Lowe - Lay Committee member Adam Lowe wrote a piece in 2017 on the results on the SMILE RCT. The first sentence of the piece identifies his negative views towards the trial into the Lightning Process: Controversial Bristol University researcher Esther Crawley, who claims to have treated children with ME/CFS by using a treatment based on two pseudosciences…. He also reports inaccurate opinions of others about the LP suggesting the approach is abusive without also presenting the	Thank you for your comment. The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-

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				facts available in the evidence base that directly contradict that opinion: 'Crawley published research recently that one former teacher claimed may constitute child abuse... Retired Deputy Head Teacher Christine Fenton…expressed the following concern about the basic conflict of Lightning Process (Crawley's most recent and controversial trial) and tenets of childhood protection: 'LP participants are directed to not talk to others about it – keep secrets – to report positively regardless of their internal view is appalling to me. Child Protection has a key tenet "secrets are not OK" – if an adult tells a youngster to keep a secret it is a form of control and creates an environment in which abuse can occur more easily.' (https://vadamagazine.com/lifestyle/health/esther-crawley-claims-harassment-university-no-record) This article identifies that he has already formed an opinion about the LP, that is not based on the evidence and should not serve on the committee due to this lack of impartiality.	ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared. The Register of interests on the NICE website sets out the declared interests of Dr Charles Shepard and the actions taken to address them. See the Policy on declaring and managing interests for NICE advisory committees for more information on how interests are managed(https://www.nice.org.uk/ Media/Default/About/Who-we-are/Policies-and-procedures/ declaration-of-interests-policy.pdf).
Register of Lightning Process Practitioners	General	General	References for comments	Beasant, L., Mills, N., & Crawley, E. (2013). Adolescents and mothers value referral to a specialist service for chronic fatigue syndrome or myalgic encephalopathy (CFS/ME). *Primary Health Care Research & Development*, 1–9. https://doi.org/10.1017/S1463423613000121 Chou, R., Aronson, N., Atkins, D., Ismaila, A. S., Santaguida, P., Smith, D. H., Whitlock, E., Wilt, T. J., & Moher, D. (2010). AHRQ Series Paper 4: Assessing harms when comparing medical interventions: AHRQ and the Effective Health-Care Program. *Journal of Clinical Epidemiology*, *63*(5), 502–512. https://doi.org/10.1016/j.jclinepi.2008.06.007 Crawley, E., Gaunt, D., Garfield, K., Hollingworth, W., Sterne, J., Beasant, L., Collin, S. M., Mills, N., & Montgomery, A. A. (2018). Clinical and cost-effectiveness of the Lightning Process in addition to specialist medical care for paediatric chronic fatigue syndrome: Randomised controlled trial. *Archives of Disease in Childhood*, *103*, 155–164. https://doi.org/10.1136/archdischild-2017-313375	Thank you for the references.

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				Davidson, R. J. (2003). Alterations in brain and immune function produced by mindfulness meditation. *Psychosomatic Medicine*, *65*(4), 564–570. https://doi.org/10.1097/01.PSY.0000077505.67574.E3 Ferrarelli, F., Smith, R., Dentico, D., Riedner, B. A., Zennig, C., Benca, R. M., Lutz, A., Davidson, R. J., & Tononi, G. (2013). Experienced Mindfulness Meditators Exhibit Higher Parietal-Occipital EEG Gamma Activity during NREM Sleep. *PLoS ONE*, *8*(8), e73417. https://doi.org/10.1371/journal.pone.0073417 Lutz, A., Brefczynski-Lewis, J., Johnstone, T., & Davidson, R. J. (2008). Regulation of the Neural Circuitry of Emotion by Compassion Meditation: Effects of Meditative Expertise. *PLoS ONE*, *3*(3), e1897. https://doi.org/10.1371/journal.pone.0001897 Parker, P. (2011). *Dû: Unlock your full potential with a word*. Nipton Publishing. Parker, P. (2012). *An introduction to the Lightning Process®: The first steps to getting well*. Hay House. Parker, P. (2013). *Get the life you love, now: How to use the Lightning Process® toolkit for happiness and fulfilment*. Hay House. Parker, P. (2020). *LP Protocol 2020*. https://doi.org/10.13140/RG.2.2.22761.72801 Parker, P., Aston, J., & de Rijk, L. (2020). A Systematic Review of the Evidence Base for the Lightning Process. *EXPLORE*, *1–30*. https://doi.org/10.1016/j.explore.2020.07.014 Parker, P., Aston, J., & Finch, F. (2018). Understanding the Lightning Process approach to CFS/ME; a review of the disease process and the approach. *Journal of Experiential Psychotherapy*, *21*(2), 8. https://jep.ro/images/pdf/cuprins_reviste/82_art_2.pdf Reme, S. E., Archer, N., & Chalder, T. (2012). Experiences of young people who have undergone the Lightning Process to treat chronic fatigue syndrome/myalgic encephalomyelitis—A qualitative study. *British Journal of Health Psychology*, *18*(3), 508–525. https://doi.org/10.1111/j.2044-8287.2012.02093.x	

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Register of Lightning Process Practitioners	Guideline	General	General	NICE guidelines have always been highly valued due to their reliance on robust evidence. Therefore, we are concerned about NICE's reputation and the options for the wellbeing of patients by the draft version of the guidelines. The draft recommendation to 'not to offer therapies derived from osteopathy, life coaching and neuro-linguistic programming (for example the Lightning Process) to treat or cure ME/CFS.' (Draft Guidelines P27 L24-P28 L 10) is of particular concern. As a high standard of evidence is required for NICE to recommend an intervention, that same standard should be applied to recommendations against an intervention. This does not seem to have occurred in this case and there is evidence, identified in specific sections of the NICE documents in our other comments, that the recommendation has been influenced by: 1. a reliance of unsubstantiated opinions over published evidence about the Lightning Process (LP) 2. a lack of impartiality and presence of bias against the LP 3. a concerning, inconsistent and biased interpretation of the evidence. With the greatest of respect, we suggest the conflicts of interest within the committee members should be resolved. This should be followed by an impartial review of the evidence with the inclusion of experts in qualitative studies and with a more complete knowledge of the evidence base for the interventions concerned.	Thank you for your comment. The NICE Policy on declaring and managing interests for NICE advisory committees sets out the processes for : • what interests need to be declared and when • how declared interests should be recorded • when a declared interest could represent a conflict of interest and the action that should be taken to manage this. As with any other guideline this Policy has been applied to this guideline. The Interests Register for the committee is published on the NICE website (https://www.nice.org.uk/guidance/indevelopment/gid-ng10091/documents) . The register has been updated throughout the development of the guideline and includes the decisions and actions made on the interests declared. See the Policy on declaring and managing interests for NICE advisory committees for more information on how interests are managed(https://www.nice.org.uk/ Media/Default/About/Who-we-are/Policies-and-procedures/ declaration-of-interests-policy.pdf). *Committee composition* The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders

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					and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					Recommendations were made in accordance with Developing NICE guidelines: The manual as well as the methods chapter for this guideline. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. When making decisions about interventions the committee take into consideration many factors including the clinical and cost effectiveness, taking into account the benefits and harms. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS '. The committee agreed that concerns raised in the qualitative evidence about the lightning process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)
Register of Lightning Process Practitioners	Guideline	General	General	Unsubstantiated opinions instead of evidence A central concern is that these guidelines appear to be based on a series of unevidenced and incorrect opinions about the LP. Over the last 21 years a number of misinterpretations and inaccuracies about the LP have been repeated on the internet and social media so often that, understandably, they have been taken as truth. The Register of LP Practitioners appreciate that there is much caution, confusion and uncertainty about interventions in the ME/CFS field and recognise it has a responsibility to help resolve these misconceptions. To achieve this, it has:	Thank you for your comment and information.

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				- Welcomed researchers, clinicians and family members/carers who wish to attend the LP as observers - Written and contributed to peer-reviewed papers and books explaining the supporting concepts and mechanics of the intervention (Parker, 2011, 2013; Parker et al., 2018, 2020) - Made the entire protocol of the LP publicly available (Parker, 2020) - Welcomed discussion of any elements of the approach with interested parties - Created, in 2006, a Register of LP Practitioners to ensure standardisation of delivery of the LP and professional accountability of practitioners. The Register provides the standardised set of LP materials, has a code of conduct and professional conduct committee and membership is contingent on ongoing compulsory CPD, evaluation and supervision. Despite these steps, these inaccuracies persist and have found their way into the draft NICE guidelines. To resolve these issues in the NICE documents it is important to have an awareness of the facts and their supporting evidence. Openness and transparency in the LP. Researchers, clinicians and family members have always been welcome to observe and discuss any elements of the LP and there is published information about how the LP works and its entire protocol (Crawley et al., 2018; Parker, 2013, 2020; Parker et al., 2018). This is aligned with the LP's patient-centred approach which encourages open discussion of the materials with family, friends and HCPs to help participants find the best way for them to make use of the tools.	

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				The designer of the LP, Dr Phil Parker, considers ME/CFS to be a physiological multisystem illness that needs a cautious reasoned approach to assist recovery. These points are evidenced in papers, books and the published protocol of the LP (Parker, 2012; Parker et al., 2018, 2020). The LP teaches people ways to influence their physiology by using brain retraining exercises based on relaxation and savouring of memories. It is not an exercise-based/physical activity approach. It advocates listening to your body signals and working out how you can use the brain retraining skills to change your physiological function (Parker, 2013; Parker et al., 2018). The LP materials and handouts specifically advise participants to avoid 'just being positive and push through' as it considers that a recipe for increasing the chance of relapse (Parker et al., 2018). A compassionate, patient centred approach. The LP is patient-centred and encourages the development of self-compassion. As a result, a large part of the LP is focused on why kindness, and not blame, is essential in recovery or training, evidenced in the three books on the process (Parker, 2011, 2012, 2013). The practitioners also work to clear guidelines that emphasise how important it is to assist participants in a kind and supportive way as they explore how to apply the LP tools in a way that works for them. The LP is a collaborative, empowering and supportive intervention. The LP helps people to realise they have some agency in helping their body make change. The first step in this is to realise mal-adaptive processes are occurring at an autonomic level in their physiology. This concept is summarised by using the constructed verb dû (Parker, 2011; Parker et al., 2018) which has been specifically designed to emphasise that these processes are not their fault. However, as they are occurring within their physiology, it raises the possibility that by using calming brain training techniques they can begin to learn to influence them. Although supported by the evidence base (Davidson, 2003; Ferrarelli et al., 2013; Lutz et al., 2008; Speer	

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				et al., 2014; Speer & Delgado, 2017), this is new for many and much time is taken exploring what the supporting evidence is for this and how to make those changes. The LP is a well-established and regulated intervention. Developed from a qualitative enquiry and modelling project in 1999 the approach has been used by over 24,000 people worldwide. The LP has a professional register of practitioners to ensure consistency of delivery and practitioner standards, a code of ethics and a professional practice committee. It has good standing with HCPs and university and medical researchers, who through collaboration have helped to explore its efficacy and to understand and improve the approach. This has resulted in developing an evidence base for its use in a range of issues including pain, fatigue, multiple sclerosis, anxiety and substance use (Parker et al., 2020). The LP, like most interventions, produces variable results but is of help to many participants. A systematic review concluded 'Although it found a variance in reported patient outcomes, the review also identified an emerging body of evidence supporting the efficacy of the LP for many participants with fatigue, physical function, pain, anxiety and depression' (Parker et al., 2020). The SMILE RCT LP reported improved outcomes when the LP was added to Specialist Medical Care, and that participants did not have any serious adverse events attributable to either treatment arm (Crawley et al., 2018). It is well-recognised that those with ME/CFS attending any intervention/consultation will expend energy and if no benefits are achieved from the intervention, could feel more fatigued. It is also well known that ME/CFS is a fluctuating condition with relapses. These unfortunate features of ME/CFS are seen in all interventions and is recognised to be a result of the condition and is not evidence of harm attributable to the intervention.	
Register of Lightning	Guideline	028	010	1.11 Managing ME/CFS 1.11.16 Do not offer people with ME/CFS	Thank you for your comment. The committee discussed the evidence for the Lightning Process and acknowledged that although some aspects of the therapy

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Process Practitioners				- Therapies derived from osteopathy, life coaching and neurolinguistic programming (for example the Lightning Process). Comment: • The evidence for this statement appears to be derived from an interpretation of a single qualitative study (Reme et al., 2012). The paper is reported on in a way that does not reflect its original findings. Furthermore, the small scale study (n = 9) has been used as evidence of 'harm', something the study was not designed to evaluate and a term that is not used in the paper. Reports of experiences such as this cannot be used to substantiate harms of an intervention. An RCT reporting Adverse/Serious Adverse Events (AEs/SAEs) is the accepted approach to evaluate such outcomes (Chou, 2010). • It is also of note that despite the reliance on this qualitative study none of the expert evidence statements was provided by those with expertise in qualitative methods. • An RCT (Crawley et al., 2018) compared Specialist Medical Care (SMC) to SMC +LP (N = 100, n = 49 SMC, n = 51 SMC +LP). The results showed a significant effect for SMC+LP compared to SMC for all measures (pain, fatigue, physical function, anxiety, depression, days at school) and, importantly, reported no Adverse/Serious Adverse Events (AEs/SAEs). • In the critique of the research in the field (expert evidence) Edwards notes 'All appear to be based on unsubstantiated theory and none validated by adequately designed trials.' However the downplaying of the RCT and prominence of some selective findings from the qualitative study identifies an inconsistency on	were found to be helpful, experiences varied. Some negative experiences were reported around the confusing nature of the educational component, the intensity of the sessions, and the secrecy surrounding the therapy. The committee were particularly concerned around the secrecy of the Lightning Process and the lack of public information on the components and implementation of the process. The committee discussed concerns that the Lightning Process encourages people to ignore their symptoms and push through them and this could potentially result in harm for people with ME/CFS. The committee noted they had made clear recommendations on the principles of energy management and this is at odds with the principles of energy management in the guideline. In addition, the committee were aware that some children had been told not to discuss the therapy with their carer or parents. The committee agreed this was an inappropriate and harmful message to give to children and young people. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H). After considering the stakeholder comments the committee agreed to remove the reference to osteopathy recognising that the recommendation should be specific to the Lightning Process and not osteopathy. In line with the review protocols we have considered RCT evidence on the effectiveness of interventions and qualitative studies of people's experiences of intervention including the Lightning Process to determine their appropriateness rather than simply reviewing descriptions of the intervention protocol. Within this framework information from a CPD programme or descriptions of the intervention protocol such as in Parker 2018 is not appropriate to base recommendations upon. Information described are not sufficient to override the committee's concerns

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				how adequately designed studies vs. qualitative interview-based studies has been valued. - The qualitative study's (Reme et al., 2012) findings were reported as, "Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved." and "Two participants reported being dissatisfied with the treatment and did not experience any improvement in their CFS, while the remaining seven reported that they were very satisfied with the treatment and that they were either much or very much better." It is important to note the lack of the use of the term 'harm' here and that is completely absent in the paper. Based on these findings it is not logical to extrapolate the experiences reported by 'a (unspecified) few' (Reme et al., 2012) of the 9 participants to the describe the delivery of the LP, as a whole, in 2007 (when the study was conducted). - The relevance of this study's findings, undertaken in 2007 (Reme et al., 2012), to delivery of the LP in 2020 is further undermined by the LP's response to its publication. As a result of this study, an audit of how practitioners were delivering the LP was undertaken. A specific CPD programme was introduced at the time to ensure effective communication of the concepts identified as potential issues in the study (Parker et al., 2018). It is therefore not appropriate to use these selective reports from 2007 to make recommendations about the delivery of the LP 13 years later. - There is an inconsistency in the way the LP has been specifically targeted by these guidelines. Other complementary approaches used by those with ME/CFS, Mindfulness (although mentioned in the Evidence review G documents P329 L 11 as 'showing harm'), Mickel, Reverse Therapy, etc. have not been	about the Lightning Process that have been based on the consideration of the multiplicity of factors described below. Studies by Reme 2012 and Crawley 2018 have been included in evidence review G and findings have been reviewed by the committee. Please note that as with all NICE guidelines, in line with NICE method processes, we do not use statistical significance to examine the clinical effectiveness of interventions but look at clinical importance. RCT evidence showed mixed findings of a benefit in terms of some outcomes but not others. Also, this evidence was limited to one RCT and was of low and very low quality. RCT findings were not downplayed but were considered alongside the qualitative evidence and the committee's clinical experience and considering its limitations. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts of the Lightning Process from the Reme study have been synthesised and contribute to different review findings that the committee has considered (such as the theme titled the 'Theory behind the Lightning Process', Peer support', 'Goal setting', 'Practice and application' highlighting aspects of the interventions that people had found helpful) However, this was not representative of the experience of all people included in the evidence for the Lightning Process. Negative experiences including statements reflecting a pressure to be happy and the encouragement not to talk about the therapy were taken into consideration as they also provide evidence of peoples' experience of the Lightning Process regardless of how many people felt this was the case. Accounts on the secrecy surrounding the Lightning Process also raised the committee's concerns about ethical consideration surrounding the Lightning Process.

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				singled out in the same way (Evidence G P 339 L11) despite the LP having a stronger and more developed evidence base supporting its use than the majority of these. These points identify that this conclusion is based on an inconsistent interpretation of the evidence base and relies on inaccurate interpretations of the reports from a single qualitative study which cannot be assumed to be representative of the LP in 2020. We suggest this statement, which is unsupported by the evidence, be removed and replaced with a reflection of the need for more research into this intervention.	RCT and qualitative evidence available was not the only source of information that the committee has considered. The committee have utilised their awareness of what people with ME/CFS experience, developed through their clinical practice to further inform decision making as well as their clinical judgment. Decision making has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee strongly agreed that there is lack of transparency about aspects of the research and the treatment protocol for the Lightning Process that has raised ethical and safeguarding concerns. In addition, the evidence for the Lightning Process was very limited and the lack of replicated research together with the committee's awareness of people's concerns about this intervention, did not support a recommendation to offer or consider offering the Lighting process and supported a 'do not offer' recommendation.
Register of Lightning Process Practitioners	Guideline	028	010	Physical activity Comment: The Lightning Process has been erroneously included in the Physical Activity section. This is not the correct category for it as it is not based on increasing physical activity. Instead, it is a mind-body approach, teaching conscious use of neurology to help influence physiology. This suggests the committee is unaware of or has not read the published evidence base describing the intervention in detail (Parker, 2013, 2020; Parker et al., 2018, 2018) Elsewhere it is included in 'Behavioural/psychological support' and not the Exercise category (e.g. Guideline P 192 L 11) identifying an inconsistency in the categorisation.	Thank you for your comment. After considering the stakeholder comments the recommendation on the Lightning Process has been moved to a separate subsection in the symptom management for people with ME/CFS section of the guideline.

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				We recommend that this inconsistency is resolved by placing it in either a category of Psychoneuroimmunological approaches, or less accurately, approaches similar to CBT or complementary approaches.	
Royal College of Occupational Therapists	Guideline	General	General	We are concerned that the guideline overall gives a negative view of this illness, stating there is no clear pathology, no cure and the shift of focus onto the severely affected may imply to both health professionals and patients that there is still no biological understanding and nothing that can be done to improve the symptoms. There is already a tendency across health and social care to dismiss the experience of patients with ME/CFS and this may lead to further disengagement in the belief there is nothing we can do.	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
Royal College of Occupational Therapists	Guideline	General	General	There is no reference to Post Viral Fatigue Syndrome and where this overlaps with ME/CFS and the emphasis of the guideline appears to be on the severe end of the spectrum with little reference with how to address PVFS or mild ME/CFS in order to prevent a deterioration, as some patients report they progressed in severity from a post viral syndrome to ME/CFS due to inappropriate advice around exercise or work earlier in their illness. There is also evidence that the illness changes over time and therefore, those with a more recent viral onset may have a different response to those with long standing illness.	Thank you for your comment. The guideline's population is people with ME/CFS and the scope did not include post viral fatigue syndrome and as such the committee were unable to make recommendations or draw comparisons to ME/CFS.
Royal College of Occupational Therapists	Guideline	General	General	There is also no reference to subgroups which have been indicated in research leaving the impression that this is a homogeneous group with one shared prognosis. In clinical practice we see a spectrum of patients from post viral/mild to	Thank you for your comment. The complexity, the heterogeneity of ME/CFS and the wide range of impact it has is acknowledged the first recommendation in the guideline.

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				very severe and a range of presentations and co-morbidities, some of whom can experience a significant improvement in symptoms whilst others continue to battle with stabilising their condition. The diversity and complexity of the illness doesn't come across clearly.	
Royal College of Occupational Therapists	Guideline	General	General	We are concerned that there is a lack of clarity in the guideline as to who is responsible for which intervention. In the previous guideline there was a section for primary care and specialist care. In this guideline it contradicts itself saying that all patients should be referred to specialist services, but then only patients with long standing or severe symptoms should be referred to specialist Occupational Therapists or Physiotherapists, and then that specialist services will have ongoing consultation around the management plan. Who is going to do key role such as the management plan, and how will these resources be funded?	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.

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					In addition the section on reviewing the care and support plan is placed in primary care. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource. Commissioners will need to consider how to fund these services and, in some areas, new investment might be required.
Royal College of Occupational Therapists	Guideline	General	General	We respect the emphasis on client centred support (though this should go without saying and also in the 2007 guidelines) the importance of thorough examination; investigations; the importance of validating the person's experience by listening to their narrative and the power of being 'believed'. Comprehensive risk assessment; educating about and highlighting the potential needs of severely affected people, inclusive of potential safeguarding issues are of course highly valued. Limiting the scope of well evidenced intervention risks setting people back on their journey of recovery (where recovery often means regaining a sense of agency and desired quality of life, not necessarily returning to pre-morbid levels of function). A number of our patients here have expressed similar concerns. There is a gap in the draft guidance of the voice and experience of professionals working in the field of ME/CFS being heard, in conjunction with those of their patients who have benefited greatly from activity management strategies, cognitive behavioural therapy and graded exercise therapy, as opposed to being confined for the long haul within their 'energy envelopes'. Language used in the guidelines risks much uncertainty about the way forward for someone with CFS/ME and disregards well researched evidenceinforming good practice.	Thank you for your comments. The committee agree that the emphasis should be on the person with ME/CFS and throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline. The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusions in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations.

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				Much is now understood about the condition, for example how symptoms may be explained through dysregulation of the autonomic nervous system, which has good scientific research and is very helpful for patients to hear and understand, providing a model to work within. If this draft guidance remains as it is, the hopes of many will be dashed and 'cautious optimism' replaced with 'considerable pessimism'. The use of language such as 'cure' and 'no cure': Under 1.11 Managing ME/CFS – the first thing you see is *"Be aware there is no current treatment or cure for ME/CFS".* This has very strong, unhelpful connotations and could result in loss of hope for both patients and GP's. Suggestion: *"while there is no medical cure for ME/CFS at the current time there is good evidence that an individual's overall quality of life and level of functioning can improve over time by using a holistic approach incorporating self-management strategies such as activity management techniques to conserve energy".* There are many other conditions NICE have written guidelines for that are 'incurable' for example Tinnitus, Diabetes, Parkinson's Disease and Multiple Sclerosis. None of the NICE guidelines for these conditions mentions the word cure. The tone of the Tinnitus guideline should be a model for how to approach the ME/CFS guideline with use of the phrase 'there are a variety of management strategies that help many people live well with tinnitus' This repeated emphasis throughout the draft guidance of the lack of a cure or effective treatments, will likely have wide reaching negative effects on an individual newly diagnosed with ME/CFS, potentially increasing the risk of a decline in their mental health. It may limit engagement for many in the therapeutic process.	The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence , in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences.

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				It risks engendering a sense of hopelessness in those with the condition, those health and social care professionals working with or encountering someone with ME/CFS and also the general public. The vicious cycle of stigma, lack of understanding, empathy and compassion will continue and amplify an individual's distress. Commissioning of much needed specialist services may be put into question when we live in an outcome based world and results for investment. Positive results when working within ME/CFS are very real, but also often very subtle and over a long term basis. It risks causing professionals who work within the challenging and highly skilled field of ME/CFS to feel de-valued when thinking in such narrow terms. · Principles of care: 1.1.1 'its pathophysiology is unclear'. There is now much known about the physiological abnormalities which are present in ME/CFS and this needs to be acknowledged in this document. There is a plethora of published research identifying evidence of changes in multiple different systems in the body. Evidence indicates that the symptoms of ME/CFS are triggered by a dysregulation in dynamic systems such as the immune system, the autonomic system, metabolic processes and neuroendocrine systems.	When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. The committee recognise that there is little representation in the literature of people who have recovered from ME/CFS and the committee would welcome research and publications in this area as this can only further inform the care and support of people with ME/CFS. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the

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				The process of dysregulation means there is not a single identifiable common factor between all people who have the symptoms of ME/CFS, however that is not the same as stating that we do not know or understand a lot of the physiological abnormalities that occur. Stating that 'the pathophysiology is unclear' strips hope away and may increase a sense of stigma, isolation and being disbelieved i.e. if there is no pathophysiology then how can the illness be real? In 1.1.2 the guideline wishes to instill a sense of belief and being believed, this does nothing to support the hoped for foundation in care of perceived compassion, care and empathy experienced by the patient. Why do we encourage people to rest regularly through the day in a pre-emptive manner for set periods of time? We encourage well planned pre-emptive resting to manage an unregulated autonomic nervous system and support homeostasis. Just encouraging rest is not helpful, there needs to be a clear scientific explanation of how rest benefits those with ME/CFS. Information and support 1.6 4: It states that *"varies in long term outlook from person to person – although a small proportion of people recover or have periods of remission, many will need to adapt to living with ME/CFS"* and "it may be self –managed with support and advice". It states a 'small proportion of people' – if you are going to write this it needs to be evidence based with percentages for adults and young people for example. Rather write '*there is a percentage of people who recover fully from this fluctuating condition; others who experience periods of remission; and perhaps a larger percentage who continue to implement self-management strategies in the longer term, thus learning to adapt*	comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect people all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.). In reference to your comment on the,' the pathophysiology is unclear' has been edited to ,'is still being investigated'. *Terms used in the guideline* After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits*. The committee noted the concept of describing the amount of energy a person has to do all activities without triggering an increase in their symptoms remains the same. • *Debilitating fatigability.* This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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				to and live with ME/CFS as is the case with many other long term health conditions' *The use of the word "may" suggests that it may not be.* A recovery model would advocate that where activity levels may well not return to pre-morbid levels, this does not discount that quality of life can be greatly improved. Why not say '*there is good evidence that it can be self-managed in conjunction with appropriate support and advice from your GP in conjunction with specialist services'.* The energy envelope 1.3: This is a term which was used many years ago in the context of managing CFS/ME and has connotations of 'restriction'. Under 1.3 Advice for people with suspected ME/CFS', it says to advise them "not to use more energy than they perceive they have – stay within their energy envelope" and "to rest as they need to". Many of those with CFS/ME would agree with this being a restrictive and limiting term, increasing a sense of fear, anxiety and extreme caution in moving beyond current baselines should they wish to. Envelopes are often 'sealed'. Advice here around rest is vague, we would talk about managing energy, by having a balance of rest and activity but to avoid resting for too long, as the body also needs to move to avoid cardio-vascular and muscular de-conditioning (which is hugely on the rise relative to COVID-19 and also home working through lack of movement and thus not specific to CFS/ME but common sense). Anyone who works in CFS/ME is aware that it is not de-conditioning which causes CFS/ME, but it is de-conditioning which then adds another limiting layer to reduced physical	*1.11.2 Boom and Bust* After considering the stakeholder comments the committee agreed to clarify that, 'energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).' It is now clearer that this avoids the 'boom and bust' pattern *Advice for people with suspected ME/CFS* Energy envelope After considering the stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on pem and energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. Rest The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of trial evidence about rest in people with suspected ME/CFS but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. As you note the committee recommend a personalised approach and this would

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				stamina and exercise tolerance, a hallmark of the condition. Limiting language once more: Under 1.11.2 – 'Energy Management' - again it uses energy envelope, and words like *"limits"* rather than capacity or current ability, which suggests a sense of movement/ progress. Also under this heading it says, "*uses a flexible, tailored approach so that activity is never automatically increased but is progressed during periods when symptoms are improved and allows for the need to pull back when symptoms are worse".* This could be viewed as 'do more activity on good days' i.e. a boom and bust approach which one would wish to avoid. The language used 1.11.2 indicates dependence on symptoms rather than, getting stability and a good baseline of activity across the week, regardless of whether it's a good or bad day. Diagnostic tests 2.1.2: The guideline has not given any indication of a minimum set of investigations; baseline bloods are no longer part of the draft guideline. These have been extremely helpful for all health care professionals when considering the possibility of other conditions causing or contributing to fatigue and of course for patients themselves. On many occasions, in the clinical setting, a doctor has noticed anomalies within someone's blood tests, which have benefited from further investigation. Many services operate without access to any investigative work so rely on all appropriate investigations being done prior to referral. Not providing any guidance on this could result in patients being under investigated and potentially treatable causes or contributors to their symptoms being missed. It could also lead to services developing their own minimum set of investigations	include discussing with the person with suspected ME/CFS about how much rest is appropriate. *Suspecting ME/CFS* Diagnostic tests Throughout the guideline the committee have recommended the importance of carrying out investigations to identify other conditions or exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis.

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				required before referral which may result in additional unnecessary tests being done: Please consider re-instating a minimum set of investigations. Some concerns about what tests are not being asked for e.g. phosphate. Phosphate can give an indication of hyperventilation which increases fatigue i.e. this test helps to build up clinical picture of patient. CRP: It is hard to make this a diagnostic marker as it is implicated in many other health conditions Inflammatory cytokines: Also challenging to make this a diagnostic marker as they vary in different studies so no consistent pattern plus same as CRP in showing up in different health conditions Two day cardiopulmonary would be helpful Differential diagnosis: There are many equally complex conditions that have symptom overlap with ME/CFS and our awareness of this is continually expanding as research progresses. Audit data and published research has demonstrated that the accuracy of diagnosis in primary care is low. This guideline does not indicate any necessity for a specialist assessment to make a diagnosis and has not provided any guidance regarding how to navigate the complexity of overlapping conditions.	*Reduction in timeline* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. As you note people with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important that this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (

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				No guidance on ruling out common misdiagnoses such as primary sleep disorders, mood disorders and primary dysautonomia (e.g. POTS). This makes it very difficult for commissioners to decide which patients should have funding for treatment in an ME/CFS service and this lack of guidance will lead to inequity of access to specialist care across the country. Suspecting CFS/ME 1.2: In 1.2.3 'The person has had all of the persistent symptoms for a minimum of 6 weeks in adults and 4 weeks in children and young people'. Although occupational therapists adhere to the concept of early intervention and prevention of decline, provisional diagnosis of ME/CFS at this stage is premature and could send someone's mental health spiralling downwards and increase risk. Far better to talk about ways of managing persistent fatigue at this stage. Time is a very important diagnostic tool in primary care; there are many conditions with symptom overlap with ME/CFS which may develop over several months e.g. endocrine disorders including Addison's disease, pituitary disorders, and thyroid disorders, coeliac disease, autoimmune conditions, lymphoma, diabetic auto neuropathy and so forth. These conditions may present initially with fatigue and other symptoms which are seen in ME/CFS; the identifying symptoms or blood abnormalities may not show up in the early stages of illness. Post viral fatigue can go on for months; though there can of course be over-lap with ME/CFS, better to take an initial 'watchful waiting approach' – this approach should not impede fatigue management strategies being suggested by the GP.	See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation and replaced with 'perpetuating ME/CFS'. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was

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				One of the major problems with managing post-illness fatigue is people's impatience to get better and return to work and exercise. Reducing the timescale for diagnosing ME/CFS undermines the efforts to promote the need for time and patience to allow appropriate convalescence after an illness; rather it implies that having fatigue 6 weeks after an infection or operation is atypical and constitutes them having a serious illness for which there is no cure. Confusion regarding when to diagnose and refer could result in an increase in referrals to specialist services for people who do not have ME/CFS, and thus take resources from those who do. This may also lead to over-diagnosis without appropriate review, if not being seen regularly by the GP and not linked in with specialist services. It also neglects the cohort of people who develop this condition gradually over many months or even years. In the clinical setting, people who have been previously misdiagnosed, but have lived their lives through the 'lens' of having ME/CFS; how do you then remove this sense of identity by reversing the diagnosis without causing further damage? Waiting 4-6 months seems reasonable and sensible. Physical activity: 1.11.16: 'Do not offer people with ME/CFS any therapy based on physical activity or exercise as a treatment or cure for ME/ CFS'. To our knowledge, specialist CFS/ME services have never stated that physical activity or exercise is a 'cure' for ME/CFS. This is totally out of context and evidently misunderstood.	important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. *Discharge* The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and

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				Such guidance is against much evidence that gentle increases in physical activity support health and function in ME/CFS, and provide (if presented appropriately) an increased sense of control when living with the condition. The largest trial of graded exercise therapy showed it significantly reduced post exertional malaise more than staying within an 'energy envelope'. A flexible approach is key and there is a clear misunderstanding of 'incremental increases' within sectors of the ME/CFS community and some GP's and other professionals; such increases are not 'fixed', however may have been interpreted as such and hence led to a crash through increasing either too quickly or in too large amounts. 10-20% are reasonable increments and well understood by our patients here within activity, either physically, cognitively, socially i.e. grading activity, not 'exercise'. Measurement is a very helpful concept when a patient is setting their short and longer term goals. People who have used a carefully graded increments approach within physical activity often state that this alongside activity management strategies has been extremely helpful. Psychological support: CBT: 1.11.43: '*Only offer CBT to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS and to reduce the psychological distress associated with having a chronic illness. Do not offer CBT as a treatment of cure for ME/CFS'*.	that it was appropriate to have a do not recommendation. (See evidence reviews G and H) *Training* The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as training costs or access to ME/CFS specialist services, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned.

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				Again there is the use of all or nothing language and highly medicalised frames of reference concerning 'treatment' and 'cure'. CBT has never been put forward as a 'cure' for CFS/ME. It is certainly used as treatment / support / intervention for many physical conditions with strong efficacy, why would be deny someone with CFS/ME this support and intervention? Why should people miss out on a potentially very helpful form of intervention through a clear misunderstanding of the intervention itself through this guidance? CBT is also extremely effective in treating co-morbid anxiety and depression in adults and children. Do not offer people with ME/CFS 1.11.16: Any therapy based on physical activity or exercise as a treatment or cure for ME/CFS . Generalised physical activity or exercise programmes – this includes programmes developed for healthy people or people with other illnesses. Any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy. Structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS.	

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				Therapies derived from osteopathy, life coaching and neurolinguistic programming (for example the Lightning Process). Many people report finding all or some of the above interventions helpful. Such statements and recommendations are not adhering to evidence based practice, relative to a well-managed graded approach to physical activity for example. The word 'cure' is mentioned yet again; anyone who works within ME/CFS would never claim any intervention to be a 'cure'. We are working with support techniques and self-management strategies to support someone in managing their condition and break the seal of their 'envelope' as it is described here, should they choose to do so. While we would not recommend some of the above interventions from an NHS perspective, choice should be respected and valued as many people have benefited from such techniques on an individual basis. The draft guidance focuses on 'what not to do' as opposed to 'what to do'. People with severe or very severe ME/CFS: 1.5.5 Resource management: Severe patients require a comprehensive physical examination and psychological assessment within limited resources. A full multi-disciplinary and multi-agency approach would be required to work with this patient group in the community. The service would require increased funding, staffing and overall resourcing to provide this type of intervention.	

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				Training needs:_Training would need to be funded and available for therapists to work with this patient group safely and effectively. Caseloads: How to define the discharge criteria for severely affected patients to allow throughput and service capacity?	
Royal College of Occupational Therapists	Guideline	General	General	The tone of the guidance appears negative and we are concerned about the impact this will have on all patients. It indicates so many things that should not be done and that nothing is curative deemed to be treatment. This creates an impression CFS/ME is an irreversible life-long disability, rather than a long-term illness which can and does improve. Change of name: There is a change in name from CFS/ME to ME/CFS, with a limited explanation as to why there is now more emphasis on ME. Changing the name in this way seems to support a lack of hope for improvement. (Page 71 lines 10-14). The draft guideline actually states Indeed it states that '*there is little pathological evidence of brain inflammation, which makes the term myalgic encephalomyelitis problematic'* yet still the recommendation is to change the abbreviation ME/CFS? Prognosis 1.6.4: Lack of data: Where is the data regarding the good prognosis for young people? Where are the stats to show the good recovery rates to give hope to patients and families? Reason for hope: Regarding adults: 1/3 recover, 1/3 improve and 1/3 do not improve - therefore 2/3 get better to some degree. The guidance indicates that no one gets better and there is no hope, which will be hugely detrimental for patients/families and those trying to provide 'treatment' for them. (Page 14 lines 22-24 & page 15 lines 1-3). 'As page 14 line 22/23 states 'although a small proportion of people recover'. People suggests both adults and young people, not just adults, this should be made explicit so	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). *ME/CFS* The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain*

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				as not to remove hope for young people. Page 15 line 2/3 states 'the outlook is usually better in children and young people than in adults'. Better than a 'small proportion' does not suggest and imply the statistics quoted above from the research. Even making a conservative estimate based on this evidence that 50%+ recover, this means the majority of young people recover, which is significantly more than a 'small proportion'. Appendix: Supporting Child and Young People document (Appendix 1) Page 17 line 4-5) The data from the survey of the 16 children and young people surveyed indicated that they want to know 'how to get better and feel better' and that experiences of this were highly valued. References: Children and young people with CFS have a significantly higher rate of recovery when compared with adults' *Carruthers, Van De Sande Mi, De Mierlier et al (2011) cited in Gregorowski, Simpson & Segal (2019).* The reported recovery in young people is between 54 and 94*% Crawley, E (2017).Young people have a mean duration of CFS for 5 years, with 68% reporting recovery by 10 years, Rowe (2019).* Recommendations for research: Professor Jonathan Edwards, UCL has expressed extensively his concerns regarding the clinical trial designs for therapy treatment for ME/CFS, particularly regarding bias, lack of blinding and subjective outcomes (Expert testimonies section Appendix 3 p6-13). It appears surprising that in the recommendations for research there isn't a focus on research methodologies for treatments (lines 21-16, p45, and p46 and lines 1-6 p47). Resources: We are concerned about references to not needing any additional resources to deliver care. There would be resource implications in:	*inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'* *Research recommendations* *Design of trials* The committee have made a research recommendation for the development of a core outcome set to improve the implementation of research in ME/CFS. The committee have included in the research recommendations on interventions the importance of long term follow-up. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted. *Resources* The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS and it is important these are addressed. There are areas that may need support and investment, such as accessing care, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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				Training: Providing training to other services to get them to a level of specialist; (Page 40 line 18) Access: Meeting the access to care guidance (see below). Key-working: Providing key-working roles. Increase in referrals: Meeting the potential increase in cases if children are referred earlier after 4 weeks of symptoms (Page 8 line 12) In fulfilling what will be an extended chasing role with Social Services re assessing for aids and adaptations (Page 72 line 20). Unrealistic expectations: We also wonder if this is setting up unrealistic expectations, to provide 'without delay' (Page 20 line 20/21), when there is a wait list (which varies depending on local authority) for all social services occupational therapy provision for equipment. Typically the wait for home adaptation assessments is approximately 12 months. Funding issues: Funding for home adaptation (disability facilities grants- DFG) is for those with permanent or long term disability, so if the mean duration for young people with CFS is 5 years (Rowe, 2019), this is not a suitable suggestion of allocation of resources (and will not meet most local authority criteria), and thus home adaptations are likely not suitable for children and young people and this should be outlined in the guidelines. Discharge 1.8.2: When to discharge: We are concerned there may be issues in discharging patients too, as there is reference to it being ok for patients to decline treatment, not attend and not to discharge if symptoms worsening. While they of course patients may decline some elements of care and attendance can be a problem, we are concerned there would be an expectation	*Discharge* The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. *Supporting people with ME/CFS in work, education and training* After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. *Financial 1.6.6* This recommendation raises awareness about advice for applying for benefits, as the person's condition changes and the care and support plan revised this would be the more appropriate time for changes in access to benefits. *Supporting people with ME/CFS in work, education and training* After considering the range of stakeholder comments the committee have revised the order of the recommendations in this section with the recommendations about support at the beginning.

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				for services such as ours to be a holding bay for CFS patients who are not making any positive changes through engagement (Page 18 line 10) Management plan: This feels positive and comprehensive. (Page 12 line 10) Access to care: We agree that flexibility should be offered re timing/length/frequency of all treatments, but this will need to be within what is reasonable for a service to operate within. (Page 17lines 1-2, 8-9) Financial 1.6.6: Page 15 line 8 'applying for benefits'. It might be helpful to include in the guidelines the importance of having a discussion with families about benefits, in particular that as young people and children are likely to improve over time, so there is a need to prepare financially for when the threshold for benefits will no longer be met. 1.9 Supporting people with ME/CFS in work, education and training: Overall this is a useful section, however page 21 lines 6/7 'some people find that going back to work, school or college worsens their symptoms'. We feel more context should be added to this statement to avoid it creating fear in those wishing to return to school, perhaps it could be stated 'if the demands are beyond the individuals current activity baseline, and reasonable adjustments can be applied to help prevent this possibility.' We believe it would be helpful to have a more positive spin, especially as there are also risks to not returning to school or college. Work: https://www.rcot.co.uk/practice-resources/occupational-therapy-topics/work Energy Management: Page 24 lines 7-24 and page 25 lines 1-3):	*Passive movements* The reference to contractures has been removed from the definition of physical maintenance. To note the physical maintenance section has been renamed to physical functioning and mobility Energy envelope After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning. *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS

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				Energy envelope: We believe the use of the concept of the 'energy envelope' is an old image, so feels like a step backwards. Restriction: The term 'envelope' suggests something sealed and potentially fixed, not a useful image for recovery. Baseline: We prefer the term 'baseline' (which is still used in the guidelines page 28 line 25 in relation to physical activity baseline). The language 'baseline' suggests a starting point for increasing activity from a point of stability, rather than something sealed/fixed and I would like to suggest this term is used in the guidelines. Importance of language: It may seem a small point, but the language we use is incredibly important in framing how we think about and feel about the treatment: 'common agreements create meanings and reality' (Hedges, 2005). Clarity: The message in the guideline appears contradictory. Energy management is not curative, it helps patients understand how not to overexert and then talks about a long term 'approach' and that it can take years to improve tolerance or activity. It suggests the first step is to reduce activity; perhaps a more useful reframe would be to ensure that booming and busting is reduced as much as possible. Sometime it is redistributing energy and activity rather than reducing; generally those with severe CFS do not need to reduce activity further. Physical activity: Page 27 lines 21-24 and page 28-29 lines 1-16: Exercise: We think it could be confusing and potentially problematic for patients to see exercise as negative and to offer new terms that make CFS completely different to other conditions that require exercise as part of their rehabilitation.	and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.

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				Passive movements: P44 line 12: This is no clear evidence that passive movements prevent contractures (Prabhu, Swaminathan, Harvey 2013) and typically the consensus now is that the most effective treatment to avoid contractures is 24hr positioning (any stretch on a muscle needs to be applied for a minimum of 8 hours), and most importantly where possible utilising active movement. Although I appreciate there is concern that physical activity does not exacerbate symptoms, particularly in those with severe CFS, this needs to be weighed up with the risks of contractures, heterotrophic ossification and the many other complications of prolonged immobility, such as pressure sores. Psychological intervention: Cognitive behavioural therapy (CBT) Page 34 lines 2-30): this is again contradictory. CBT when employed in the care of someone with CFS/ME is not a treatment or cure, but is designed to increase wellbeing, quality of life and functioning. References: • Carruthers BM, Van de Sande MI, De Meirleir KL et al (2011) Myalgic encephalomyelitis: international consensus criteria. Journal of Internal Medicine 270: 327-338. • Crawley E (2017) Paediatric chronic fatigue syndrome: current perspectives: Paediatric Health Medical therapy, 9:27-33 • Gregorowski A, Simpson J and Segal T (2019) Child and adolescent chronic fatigue syndrome/myalgic encephalomyelitis: where are we now?	

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				- Hedges F (2005) Social constructionist approach to emotion and self. An introduction to Systemic Therapy with Individuals. - Prabu RKR, Swaminathan & Harvey LA (20130) Passive movements for the treatment and prevention of contractures. Cochrane Database of Systemic Reviews. Rowe KS (2019) Long term follow up of young people with chronic fatigue syndrome attending a paediatric outpatient services. Front Paediatrics 7:21	
Royal College of Occupational Therapists	Guideline	General	General	1.1 5-6 while the pathophysiology is unclear, there are numerous studies reflecting the biological nature of the condition although not one overarching explanation. Research in chronic pain suggests a model of a dysregulated system can be helpful for clinician and patient understanding and self-management. Specialist ME/CFS services are using this type of pragmatic explanation to support patients and formulate management plans. There is a danger in not defining more clearly that ME/CFS becomes "medically unexplained" and is treated under mental health services. 1.1.3 Approach to delivering care Overall while emphasising understanding of the condition, it is not hopeful nor does it offer a goal focussed approach that is typically used in long term conditions. Very little is made of the emotional and social impact. L3. Heath professional realises it is not "just feeling tired" and asks questions that draw out the wide variety of symptoms and how they impact. Health professional is also aware of the impact of the symptoms, consequences and the length of time someone	Thank you for your comment. In reference to your comment on the,' the pathophysiology is unclear' has been edited to 'is still being investigated'. The principles of care for people with ME/CFS section of the guideline raises awareness about the challenges that people with ME/CFS have reported when accessing health and social care services (see evidence reviews AXX). In later sections of the guideline approaches to care and the impact of ME/CFS are addressed in detail. *Care and support plan** The development of the personalised care and support plan is addressed in the section on assessment and care and support planning by a ME/CFS specialist team. The plan is developed in collaboration with the person with ME/CFS and explores their aims and the management of their health and well-being within the context of their whole life and family situation. It should be proportionate, flexible and coordinated and adaptable to a person's health condition, situation and care and support needs

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				experiences symptoms on mood, self-esteem and anxiety about the future. Health professional offers hope despite there being no medical treatment, there can be some symptomatic relief and self-management can help someone feel better than they do currently. Confirm that the symptoms are recognisable and follow a distinct pattern seen in millions of cases around the world and at least 250,000 in the UK. Provide opportunities to hear others stories and meet other people with ME/CFS many of whom are living meaningful and enjoyable lives despite this condition. 1.1.5 L 15-18 and 1.5.2 L10 "Explain to people with ME/CFS and their family or carers that they have the right to decline or withdraw from any part of their management plan and it will not affect other aspects of their care. They can begin or return to an intervention if they feel able to resume". There are a number of questions and points to consider around this: Who makes the management plan? There should be a collaborative plan based initially on establishing what has happened, what is currently happening and developing a useful understanding of the condition including education about the nervous and immune systems; sleep science and the post exertional need for recovery along side validation and connection to others.	Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) Advice for people with suspected ME/CFS Section 1.3 refers to people with suspected ME/CFS. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence on advice for people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. The committee agreed it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and this advice would not result in harm to anyone. As you note the committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about how much rest is appropriate. Review date The Review in primary care section recommends at least once yearly reviews and gives further detail on the review. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. These points are made in the guideline and for this reason your suggestion has not been added to the recommendation. *Supporting people with ME/CFS in work, education and training*

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				(1.5.2 l 10-12; 1.5.3 L 9-10) The management plan needs to holistic and goal based. The health professional is facilitative not directive and provides information, support and hope. The goals need to be important to the individuals values and roles and be based in tangible activity. (e.g. I want to give my children breakfast 3 days a week, to do that I will follow a specific sleep management plan including medication, times to go to bed, get up and I will schedule rest after breakfast. I will discuss with my family what they will do and what I will do). The plan will be reviewed within the family and then with the therapist after a period of time where not only the achievement or challenges of the goal are discussed but what has been learnt and how the experience can relate to other areas of life. A management plan like this is entirely run by the patient and their family, the therapist role is to elicit the values and help the individual identify their roles. Then support, encourage guide, help with setting realistic goals and perhaps breaking it down further. Challenges in achieving can be seen as learning points and may need to be entirely changed. The patient is in control of this at all times and the health professional asks how the service can support them- this could be varied (and resource dependent) but may include regular phone or video calls; outpatient appointments; being part of a group that supports and reflects on this process of self managing. In this process referrals may need to be made and facilitated for example to social care. Additional principles for those in work: Heath professionals should be aware that 90% of people with Me/CFS will be struggling with work. Questions about work, including travel to work will elicit the nature of the challenge. For this in work, the management plan needs to account for this and additional support and resources may be required (see below) For financial	After considering the range of stakeholder comments the committee have revised the order of the recommendations in this section with the recommendations about support at the beginning.

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				and other reasons, work may be the main priority to the detriment of other areas and emotional support as well as practical changes at work may be required. Research suggests that work will not be addressed unless it is done so explicitly. Occupational Therapists can offer expertise in this area of self-management. 1.3 L 17-20 this is quite vague and does not account for post exertional symptoms following periods of activity when there are no or very few symptoms. More explicit direction might be helpful- e.g. Because of the post exertional nature of the fatigue, it is helpful to be strategic in how you approach things e.g. look at what you want to do in a week, prioritise what is important to you and what is possible bearing in mind your symptoms and your need to recover and plan when they will happen. Have periods of time when you rest even if you aren't experiencing symptoms as part of an overall strategy. L21 add in- maintain a sleep routine 1.5.3 L1 The plan is collaborate and health professional is facilitative drawing out goals and hopes as well the persons current physical, cognitive, emotional, social and domestic situation and experience. 1.5.3 9-10 addition- plan a review date, and how the review will be done- see above 1.64 22-24 Management techniques mean it is possible to live a full and valued life despite the condition. 1.6.4 25-27 There are a number of ways they can be supported with this adjustment that can include psychological support. 1.9 Supporting people in work, education and training	

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				L4 – The language used is negative and does not offer a constructive way forward; for employment suggest: Employment and education are important and significant activities in everyone's life and how the person addresses them needs to be central to their management plan. Ascertain their current situation- attendance past and current; their relationship with their manager; length of time in the organisation etc. How they feel about their work; physical, cognitive and emotional challenges including journey to work and activities that facilitate work (meals, laundry, child and animal care) as well s their actual work. Link with self-management strategies- sleep/rest routine, baseline of activity, emotional management etc what can be changed privately first. Then consider what may help within the workplace that can be negotiated either as a reasonable adjustment or flexible working policies. In some cases it may be that the person needs to reduce hours and role significantly or completely leave a job. This is the individual's choice and the health professionals can provide practical and emotional support and signpost to relevant benefits, careers and employment advice agencies. 1.9.2 liaising on the persons behalf may not be possible or appropriate and if done, should not be done without supporting the person firstly self-advocate (perhaps using reports and documents written with the health professional)	
Royal College of Occupational Therapists	Guideline	001	General	The section on Covid 19 suggests that CFS/ME is only an illness of fatigue, whereas there has been overlap of several symptoms. Wording could be changed to simply symptoms. Not focus so heavily on fatigue.	Thank you for this comment. Fatigue has been removed from this sentence.
Royal College of Occupational Therapists	Guideline	001	009	By writing encephalopathy in a bracket it is unclear that this is only relating to myalgic encephalopathy.	Thank you for your comment. Myalgic has been added to encephalopathy.

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Royal College of Occupational Therapists	Guideline	004	006	Question 1: The statement that the pathophysiology is unclear implies that there is no known evidence of biological changes. Although the underlying mechanisms need elucidating, there is evidence and increasing agreement as to the range of physiological changes that occur in people with ME/CFS. It is generally considered as a systemic disorder with neuro-immune involvement. There is a need for the guideline to reinforce this and that there is evidence of changes such as to autonomic functions, immune and inflammatory responses and changes in the anaerobic threshold. Therefore, it would be more accurate, helpful and validating for professionals and patients to indicate the body systems that are known to be involved such as the HPA axis, autonomic nervous system, immune system, metabolic systems so that health professionals have greater understanding of the dysregulation and systems affected by the illness. theory-model-oct-2020-95446.pdf (yorkshirefatigueclinic.co.uk) If this were achieved, it would facilitate a significant change in practice and prevent the current inappropriate categorisation of ME/CFS in some locations under mental health services.	Thank you for your comment. After discussing in detail the wording of this recommendation the committee agreed to edit 'unclear' to ,' and its pathophysiology remains under investigation' to clarify that there is not enough evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research.
Royal College of Occupational Therapists	Guideline	005		Page 5 section 15. 1,1.5 - Emphasising that people are encouraged to have a dialogue with their therapists about any aspect of rehabilitation they are unsure about be more useful as this would allow any anxieties to be explored as well as the rationale of why certain aspects have been selected to assist them in their management plan.	Thank you for your comment. The committee agree that the relationship between people with ME/CFS and health and social care professionals is critical and this is raised in recommendation 1.1.3. Recommendation 1.1.5 is supported by Evidence review A and xxx that some people with ME/CFS have felt there was little collaboration about the interventions offered to them. The recommendation is to reassure people with ME/CFS that they have the same right as any other person to be involved in discussions and make informed decisions about their care.
Royal College of Occupational Therapists	Guideline	005	020 - 026	This also applies to adults.	Thank you for your comment. The committee agree and recommendation 1.1.2 refers to all people with ME/CFS.

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Royal College of Occupational Therapists	Guideline	005	010	Question 1: This recommendation will be challenging in practice as without a diagnostic test it is difficult in clinical settings to separate ME/CFS of short duration from other health disorders. Many patients who report these symptoms may be having a protracted reaction to other factors, such as hormone changes, viral infections, orthostatic intolerance following a period of illness, etc. We see many people in specialist clinics at around 6 months who have a post viral fatigue syndrome which with advice on convalescence and energy management improves, however, under this guideline they will now be told they have a suspected long-term condition with no cure after only a few weeks of symptoms. As detailed later one of the difficulties with early diagnosis is that it can affect the accuracy of diagnosis as other factors require time to be eliminated as potential causes for symptoms. Rather than early diagnosis – Timely and accurate diagnosis is more appropriate.	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity.
Royal College of Occupational Therapists	Guideline	006	008 - 011	Six weeks of persistent symptoms, but also relapsing symptoms (as per ICD-10).	Thank you for your comment. 'Symptoms' here refers to type of symptoms that people with severe or very severe ME/CFS may experience. The duration is not relevant. To note, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
Royal College of Occupational Therapists	Guideline	006	028	This entire section is disabling in focus. The language focuses on what people cannot do (which can often be overcome with appropriate support and therapeutic intervention) rather than showing how people can be supported to maintain and increase independence.	Thank you for your comment. This section highlights the difficulties that people with severe or very severe ME/CFS may have and is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise

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					awareness about these difficulties and the support that may be needed to manage their symptoms.
Royal College of Occupational Therapists	Guideline	007	002	The guideline states at a 'level of their choice' we would recommend also including using the method of their choice; for example, some people prefer to use email rather than face to face interaction or prefer to be given information in pre-recorded videos they can play in short sections when they are able to manage this.	Thank you for your comment. The committee agree that flexibility in accessing services is important. In the access to care section of the guideline the committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
Royal College of Occupational Therapists	Guideline	007	004	People are only 'housebound' or 'bedbound' (which is old-fashioned language in itself, and not necessarily appropriate) due to disabling factors in the physical environment. These barriers can often be overcome with appropriate equipment and adaptations – not just support from another person. The focus here should be on enabling independence, not just 'doing for'. Suggested re-wording: *May require support, equipment and / or adaptations to participate in activities of daily living at home and in the community*	Thank you for your comment. The level and type of support needed is individual to the person and agreed as part of their personalised care and support plan. The recommendation refers to support, this does not infer support from another person. The section on aids and adaptions provides further information on equipment.
Royal College of Occupational Therapists	Guideline	007	008	We are concerned that the example only cites wheelchairs which implies that aids/equipment are only for mobility. The main equipment used by our severely affected patients are profiling beds or recliner electric chairs which support improvement of orthostatic tolerance. It would be useful to extend the examples so that the focus isn't just on wheelchairs as this can reinforce misconceptions, as some patients don't have the sitting tolerance to use wheelchairs. The need for aids and adaptations to maintain independence extends far beyond wheelchairs, and should be reflected here. Suggested re-wording: • *aids to assist mobility and independence in activities of daily living*	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information.

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				home adaptations to reduce barriers to independence in activities of daily living	
Royal College of Occupational Therapists	Guideline	007	009	Disabling language. Suggested re-wording: *may require support or equipment to facilitate communication, including use of a chosen person to advocate and communicate on their behalf*	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms without minimising the impact they have but also that it was important to highlight the support that may be needed to manage them.
Royal College of Occupational Therapists	Guideline	007	014	Disabling language. Suggested re-wording: *may require support or equipment to access information, for example due to difficulty with screens, noise and light sensitivity, headaches affecting their ability to read, or brain fog affecting their concentration.*	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms without minimising the impact they have but also that it was important to highlight the support that may be needed to manage them.
Royal College of Occupational Therapists	Guideline	007	017	As above, this jumps straight to an assumption that people will need to be cared for, rather than supported to maintain independence where possible. Suggest adding a new section before this one, as follows: *People with severe or very severe ME/CFS can benefit from person-centred therapeutic interventions to increase their independence in activities of daily living and reduce their need for additional care and support. These interventions should be provided by suitably qualified health and social care practitioners such as occupational therapists, physiotherapists, speech and language therapists and dieticians.*	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms without minimising the impact they have but also that it was important to highlight the support that may be needed to manage them.
Royal College of Occupational Therapists	Guideline	008	008 - 009	The baseline investigations to rule out other conditions should be above assessment of wellbeing. Also it should be made clear that the wellbeing assessment is for secondary symptoms.	Thank you for your comment. The parts of the assessment are all required for suspecting ME/CFS and are not in any order of priority.

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				Assessment should also include an assessment of baseline and current function in everyday activities	The assessment of baseline and current function in everyday activities is included in a clinical history. This bullet point now has some examples, including overall physical health.
Royal College of Occupational Therapists	Guideline	008	Box 1	Reduction in ability to complete occupational, educational, social and personal activities (ICD 10)	Thank you for your comment. This is included in the bullet points above Box 1.
Royal College of Occupational Therapists	Guideline	008	009	There is no list of baseline investigations. In clinical practice practitioners use the current list to ensure that primary care have completed recommended tests and excluded other possible diagnoses. It is important to specify tests to ensure that GPs are aware of the minimum requirement. Our clinic will regularly have referrals where these have not been sufficiently completed and must be reinforced and on regular occasion abnormalities are identified and require treatment. If no indication is given from a central guideline about what is required, there will be far less justification for multiple investigations. In general practice having clarity and simplicity about the necessary investigations will streamline the process and improve the likelihood of the necessary investigations being completed. Not having these guidelines will lead to abnormalities and treatable causes for symptoms being missed, and people having a label of ME/CFS, which the guideline implies is an incurable lifelong condition. It is not stated in detail which baseline investigations should be completed to exclude other diagnoses. If these are not mandatory or stated clearly there may be a variance in what GP's will investigate prior to referral and also within what time frame.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
Royal College of Occupational Therapists	Guideline	008	010	Question 1: Suspecting a long-term condition after 6 weeks in adults or 4 weeks in children of symptoms is very premature. There are multiple medical reasons for example post-virally or post-surgically that would be could be temporary and recovery, but using this criteria lead to both the clinician and patient suspecting a lifetime diagnosis which by the terms of this	Thank you for your comment. The period of a minimum of 4 and 6 weeks is to alert clinicians to the possibility of ME/CFS. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may

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				guideline has no cure, and for which no indication regarding any recovery or prognosis is given. We are, therefore, concerned about misdiagnosis and that this may stop further investigation of possible pathology too early Although it is stated that investigations will continue what is the benefit to diagnosis at this time point?	prevent them getting worse as early as possible. However after considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted. The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. • Further investigation/differential diagnoses. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.'
Royal College of Occupational Therapists	Guideline	008	011	Six weeks of persistent symptoms, but also relapsing symptoms (as per ICD-10).	Thank you for your comment. Use of the word persistent (defined as 'continuing to exist or occur over a prolonged period') includes the possibility of relapsing symptoms.
Royal College of Occupational Therapists	Guideline	008	014	Occupational in this sense is presumably meant to mean work and therefore should say 'work' as it is unclear	Thank you for your comment. The committee consider that occupational is understood in this context and would not any further clarity. For this reason your suggestion has not been added.
Royal College of Occupational Therapists	Guideline	008	016	There are multiple occasions where ME/CFS occurs without a specific onset	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in

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					recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong.
Royal College of Occupational Therapists	Guideline	008	017	Stiffness on waking is not a commonly seen symptom of ME/CFS, although patients may experience it through comorbidities, it is not identified where in the evidence where this has arisen from	Thank you for your comment. Stiff on waking describes the difficulty that people with ME/CFS have in getting out of bed after sleeping. In the committee's experience this is commonly described in people with ME/CFS.
Royal College of Occupational Therapists	Guideline	009	002	Question 1: We are concerned that there is an overemphasis on diagnosing ME/CFS and no mention of excluding other possible diagnoses that present with the same symptoms. Previously other conditions that produce the same symptoms could exclude you from the diagnosis, as it was dependent on no other medical conditions explaining the symptoms. Under this guideline patients with a broad range of conditions that produce similar symptoms, including joint hypermobility syndrome, fibromyalgia, postural orthostatic tachycardia syndrome, mast cell activation syndrome, Autism, chronic depression, trauma, and severe anxiety can now meet criteria for ME/CFS. It is often challenging in practice to differentiate between those patients whose symptoms are related to another medical condition from those who have co-morbidity with another disorder. If someone has a diagnosed long-standing health condition that is recognised to produce physical and cognitive fatigue and unrefreshed sleep are we now diagnosing this as ME/CFS? We often find in clinical practice that there is a difference in the experience of post exertional malaise in these groups. In patients with ME/CFS they are more likely to report immune related symptoms and feeling flu-like or acutely unwell after exertion, with the worst point being 24-48 hours afterwards.	Thank you for your comment and information. Throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS includes the examples you have listed. In addition the committee have added to the criteria for suspecting ME/CFS 'and where 'symptoms are not explained by another condition'. The committee agree these symptoms in the criteria are seen in other conditions, but note it is the combination and the interaction

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				In patients with other disorders, such as POTS, fibromyalgia or depression they often report increased fatigue or pain after exertion, which is at its worse directly after exertion but can have prolonged effects. Changing the emphasis from malaise (feeling unwell) to post exertional symptom exacerbation will increase the number of people coming under this diagnosis. We see some patients who have had a diagnosis of ME for many years and when we assess them, they have another condition, such as POTS, and when this is appropriately treated the symptoms improve.	of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. To note, after considering the comments made by stakeholders about the potential for misunderstanding the committee agreed to change *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE.
Royal College of Occupational Therapists	Guideline	009	002	Question 2: There will also be significant cost implications. There is already considerable pressure on specialist services to accept patients with other health conditions who experience cognitive and physical fatiguability and poor sleep. If all of these patients will now be diagnosed with ME/CFS this will dilute the focus on the specific neuro-immune nature of ME. There are also issues about skills and resources if professionals are being asked to provide care for patients who would currently be managed under mental health services, such as trauma related physiological symptoms, neurological symptoms related to autism, or biological symptoms of longstanding depression which meet these criteria.	Thank you for your comment. You have sign-posted the list of additional symptoms that people with ME/CFS frequently experience but which are not diagnostic. It is not expected that people with these symptoms will be diagnosed with ME/CFS unless they also have the four diagnostic criteria. These diagnostic criteria are more specific than those stated in the previous guideline and therefore this is not expected to require an increase in resources.
Royal College of Occupational Therapists	Guideline	009	019	In the last guideline there was a section for advice that can be given in primary care. Primary care staff often have less confidence in giving specialist advice and giving a clear list of areas to cover at the initial stage enabled specialist services to direct GPs to the guidance they can offer. There seems to be in this guideline an expectation that GPs will read the whole guideline and from this have the knowledge to explain this illness and manage the symptoms, which is unrealistic. It would be helpful to have a clearer outline of the role of the GP/primary care that is realistic to the short duration of contact time that they will have with each patient. There is a danger that primary care leave advice to specialist services, if there is then waiting lists this will delay vital basic advice around rest, sleep and fluid/nutrition.	Thank you for your comment. Recommendation 1.2.5 advises the clinician suspecting ME/CFS (this would usually be a GP) to give the person the advice in section 1.3. This includes advice on rest, fluid and nutrition.

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Royal College of Occupational Therapists	Guideline	010	017	We are concerned about the psychological impact of telling people with symptoms that they have suspected ME at such an early stage. Would this be done with other chronic health conditions without the input of a specialist? In clinical practice we see patients who resist being told they have ME as they perceive this as being told they will be disabled long term with no hope of recovery. We agree with giving early management advice for the symptoms of fatiguability, post exertional malaise and sleep issues. Advice on fatigue, pain and sleep can be given in primary care without a diagnostic label. So, we would consider it more helpful to focus on the symptoms in early intervention and reserve the diagnosis as some patients will improve with the correct early intervention.	Thank you for your comment. After considering the stakeholder comments on early diagnostic labels the committee have amended the wording in the earlier section on suspecting ME/CFS to remove the recommendation on making a provisional diagnosis of ME/CFS. However the committee agreed it was important to provide advice for people with suspected ME/CFS at this stage recognising that some people may not be diagnosed with ME/CFS. The committee agreed the advice would not be harmful in the short term either to people that are later diagnosed with ME/CFS or those that are diagnosed with another condition.
Royal College of Occupational Therapists	Guideline	011	011	Make it clear that information must be given at the time of the provisional diagnosis	Thank you for your comment. Recommendation 1.2.7 includes this and links to section 1.3 on advice for people with suspected ME/CFS.
Royal College of Occupational Therapists	Guideline	011	020	Regular rest to pace activities. Ensure the rest is both physical and cognitive.	Thank you for your comment. There is further detail on energy management and rest in the managing ME/CFS and symptom management section of the guideline.
Royal College of Occupational Therapists	Guideline	012	003	Impact on everyday activities (suggested re-wording): *physical and occupational functioning*	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Royal College of Occupational Therapists	Guideline	012	017	Equipment for everyday activities not just mobility	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Royal College of	Guideline	013	009	Question 1: If this is from suspected diagnosis where will GPs get this 'accurate up to date information' and will they have time to tailor it to each individual patient's needs?	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health

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Occupational Therapists					and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. . All patients should receive personalised information and this should be available as part of their care planning. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Royal College of Occupational Therapists	Guideline	013	012	Question 2: Although many occupational therapists provide home visits and work with those who are severely/very severely affected this would be a change to practice for many specialist services who are not funded and have insufficient resources to provide this. Also working with this group is very different to those will less severe symptoms, due to comorbidities, increased level of sensitivities and extremely low tolerance levels. There is more time required for non-direct contact activities, such as liaison with other services and family/carers. Many practitioners even in specialist services will not have experience in this area and we feel there would need to be access to more experienced practitioners for specific training and supervision which would incur further costs. Many commissioners currently will not fund this area of work as it is expensive per person with limited health outcomes. Moderate to be provided home visit or virtual appointment if it is necessary based on their symptoms	Thank you for your comment. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. *Training* The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.

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					The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs and access to ME/CFS specialist services, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.
Royal College of Occupational Therapists	Guideline	013	016	Information should be adapted to their level of cognitive ability and should be kept short.	Thank you for your comment. The link to the NICE guidelines on patient experience in adult services has further information on communication an includes about level of cognitive ability.
Royal College of Occupational Therapists	Guideline	013	022	We are concerned that this statement only focuses on recovery or adaption, and not possible improvement. We agree that it is important to recognise the experiences of patients who have had negative experiences of healthcare or felt that therapy was detrimental, but it is equally important to recognise those who have reported positive change, which doesn't mean return to previous health but is still of value. We are concerned that there is no reference to substantial health gains that some people do report. People need hope of potential improvement or reduction in the impact on their quality of life with any health condition. Whilst it is acknowledged that surveys in clinical practice are not equivalent to evidence from randomised controlled trials, they reflect the realities of the clinical care environments and diversity of patients that the guidelines are designed for. 1. Collin SM, Crawley E. Specialist treatment of chronic fatigue syndrome/ME: a cohort study among adult patients in England. BMC Health Serv Res. 2017 Jul 14;17(1):488. 2. Broughton J, Harris S, Beasant L, Crawley E, Collin SM. Adult patients' experiences of NHS specialist services for chronic	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of

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				fatigue syndrome (CFS/ME): a qualitative study in England. BMC Health Serv Res [Internet]. 2017 Jun 2 [cited 2020 Dec 2];17. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5457632/	people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
Royal College of Occupational Therapists	Guideline	013	028	It would be also be useful to include issues around hormonal changes, surgery or medical treatments, or increased demands.	Thank you for your comment. The committee discussed the inclusion of trigger events and decided on reflection to remove the examples recognising the difficulties of providing list. The examples have been replaced by the wording' these can be known or new triggers or in some cases there is no clear trigger.' to be more inclusive.
Royal College of Occupational Therapists	Guideline	014	025 - 027	Disabling language. Suggest changing line 27 to: *so they may need support and interventions to maintain their roles and activities*	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet point and hope this addresses your point: • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Royal College of Occupational Therapists	Guideline	014	022	Varies in the long term outlook from person to person: Although a small proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS We are concerned about the wording used in this paragraph and quantifying with the word "small". For those that are newly diagnosed it increases worry and abolishes all aspect of hope which is vital towards recovery. The ME association suggests that professionals "provide advice that is both optimistic and realistic". In our experience using the terminology "recovery" can be helpful. Explaining that this is different to clinical recovery (which some people make) but in a sense of personal recovery; recovery being individual to the person but being able to live a meaningful life within the context of a health condition and things being "better than they were before".	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your points: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.

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Royal College of Occupational Therapists	Guideline	015	012 - 015	Social care is more than just care packages. Occupational therapists working in social care settings provide interventions including provision of equipment and home adaptations that can help people with ME/CFS maintain their independence in ADLs and reduce the need for care packages. Suggest additional section: *Explain that social care services may also be able to provide support such as the provision of equipment to help the person living with MS/CFS to complete activities of daily living and maintain their independence.*	Thank you for your comment. The section on maintaining independence later in the guideline includes recommendations on aids and adaptions.
Royal College of Occupational Therapists	Guideline	016	005	Safeguarding we agree and follow these guidelines in practice	Thank you for your comment.
Royal College of Occupational Therapists	Guideline	017	020	Access to care we agree and follow these guidelines in practice. This paragraph is related to health not just care.	Thank you for your comment.
Royal College of Occupational Therapists	Guideline	018		Page 18. 1.8.2 - don't discharge if they DNA. This has to be considered for each individual in the context of the knowledge about their symptoms pattern, motivation and history. People should certainly not be discharged without an exploration of the reasons underpinning the DNA.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and have included discussion of the reasons in the recommendation.
Royal College of Occupational Therapists	Guideline	018	024	Also include working with carers, either family or paid agencies	Thank you for your comment. The section on awareness of severe or very severe ME/CFS and its impact includes information on supporting communication with an advocate.
Royal College of Occupational Therapists	Guideline	018	025	Question 1: We agree that these measures would be beneficial and currently rarely happen. There may be issues about how this is implemented due to lack of understanding in acute care, environmental and resource constraints. Also, communication between staff in an acute setting is more difficult.	Thank you for your comment and information.

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Royal College of Occupational Therapists	Guideline	019		The suggestion about managing inpatient care ...really should be for ALL inpatients (including less severe ME/CFS patients), not just severe/very severe ME/CFS patients. It is good that the adverse impact of strong stimuli of all types on many ME/CFS patients is highlighted. However how might 'smells' be managed on a ward? The suggestions need to be realistic and perhaps could be revised to say minimising strong smells in close proximity to the patient should be recognised.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or hospital can be difficult. This section does make a recommendation for all people with ME/CFS and includes that any difficulties in accessing hospital care should be discussed and gives some examples of what should be considered. These are expanded on for people with severe or very severe ME/CFS taking into account there are further challenges to consider. The committee acknowledge that these may not be always achievable but they should be considered and addressed where possible.
Royal College of Occupational Therapists	Guideline	019	009	There is no reference in the guideline to inpatient care specifically related to ME/CFS. There are cases where people who are severely/very severely affected require periods of inpatient care to address aspects of their health, such as investigations, medical interventions for specific symptoms/comorbidities, they require nursing support over a 24 hour period during a relapse or are in a position where their medical needs can't be cared for at home. Currently there is only one NHS facility in the UK that states that it specifically caters for severe/very severe CFS/ME. This is an important omission from the guideline, and it needs to be clear what specialised inpatient services should provide in addition to improving admission into a general hospital setting.	Thank you for your comment. The committee agree that access to services for people with ME/CFS is very important and have reinforced this throughout the guideline. They agree there is variation in the delivery of some of the recommended services across the NHS including the provision of inpatient care for people with ME/CFS. The guideline addresses access to hospital care in the access to care section and also includes recommendations for people with severe or very severe ME/CFS. There was no evidence identified in any of the reviews on the provision of specialist inpatient care and the committee were not confident in making service delivery recommendations in this area.
Royal College of Occupational Therapists	Guideline	020	020 - 022	As above, assessment for aids and adaptations should be completed by a suitably qualified professional e.g. an occupational therapist (for complex cases / needs) or a trusted assessor or therapy assistant with appropriate supervision (for straightforward cases / needs)	Thank you for your comment. The committee agree any assessment should be someone undertaken or supervised by a professional who is trained to do so. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering

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					care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Royal College of Occupational Therapists	Guideline	020	023 - 025	Guidance on providing adaptations in a timely manner can be found in *Adaptations Without Delay* (RCOT, 2019)	Thank you for this comment and information We will pass this information to our resource endorsement team. More information on endorsement can be found here **https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme**.
Royal College of Occupational Therapists	Guideline	020	002 - 003	This assessment should be carried out by a suitably qualified professional – i.e. an occupational therapist	Thank you for your comment. This recommendation lists as a minimum the areas that should be assessed and not the specific assessments that would be done by specific healthcare professionals. Depending on the individual different assessment will be required. The committee agree any assessment should be someone undertaken or supervised by a professional who is trained to do so. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Royal College of Occupational Therapists	Guideline	020	011	Environmental change to encourage energy conservation	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.

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Royal College of Occupational Therapists	Guideline	020	017	A significant issue for anyone receiving care in the home is the variety of carers and lack of training for them. Patients are often left to try to educate the carers themselves. Where will resources come from about how to care? We find care is often more successful when there is a limited number of carers involved who are familiar with that person's needs and sensitivities. Although this can be facilitated through direct payments, due to the impact of cognitive and social activity many patients with severe/very severe ME/CFS are unable to manage the recruitment and management processes involved and there are often no support services available to complete this for them.	Thank you for your comment. The committee agree that carers should be trained, the training for health and social care professionals section of the guideline the committee has recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline. In addition, in the section on the Care of people with severe and very severe ME/CFS the committee have recommended that care should be carried out by practitioners who are known to the person where possible and aware of their needs.
Royal College of Occupational Therapists	Guideline	020	019	Question 2: Aids and adaptations are not provided by specialist services and there is no funding or access to equipment suppliers to provide this. Local authorities have their own systems and funding priorities regarding provision. Some equipment that is useful to people with severe needs such as profiling beds, recliner chairs, stairlifts will not necessarily be funded or have prolonged waiting lists for assessments and provision.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.
Royal College of Occupational Therapists	Guideline	021	003	It needs to be recognised that specialist therapists can support people with reasonable adjustments and that phased return to work/education for this group needs to be managed over a longer period of time. It would be beneficial for the guideline to include that home working and flexible hours can be beneficial for this group. In our experience particular types of work, such as shift work, constant demands or deadlines can exacerbate symptoms, whilst other work environments can be more conducive, such as flexible working, having control over demand and ability to rest. Occupational Therapists can support people with considering changing work roles to more suitable working environments.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. . Education, training or employment support needs is included in the care and support plan. The recommendations are directed at the health or social care professional discussing the person's needs and this can include occupational therapists.

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					In reference to providing specific advice in the recommendations the committee note that any advice would be personalised and relevant to the person and have not added examples of adjustments that can be made.
Royal College of Occupational Therapists	Guideline	021	004	Some patients may need support with going through ill health retirement processes.	Thank you or your comment and information.
Royal College of Occupational Therapists	Guideline	021	008	It should be acknowledged that absences are related to disability and managed under the relevant disability policies.	Thank you for your comment. In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.
Royal College of Occupational Therapists	Guideline	022	005	Occupational therapists often provide support and recommendations around exam considerations and phased returns to school when appropriate.	Thank you for your comment and information.
Royal College of Occupational Therapists	Guideline	022	015	Question 1: Currently most patients do not have social care involvement, even in our severe patient groups few of them have access to a dedicated social worker so this would have significant implication on practice to involve social care across all levels from mild to very severe.	Thank you for your comment. Your comments will be considered by NICE where relevant support activity is being planned'.
Royal College of Occupational Therapists	Guideline	022	017	Question 3: A significant part of the role of specialist care is helping people to understand their condition and the factors that impact on their symptoms. In our specialist service we have an introductory session for patients and their carers to provide information on understanding ME/CFS and the dysregulation model and how this relates to the management techniques. The Yorkshire Fatigue Clinic would be willing to share its therapy model with the NICE learning database.	Thank you for your comment and this information. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme..

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Royal College of Occupational Therapists	Guideline	023	005	Question 1: The implication is that all patients will have ongoing direct clinical consultation with a specialist team, even when they are managed in primary care, this would have significant implications for resources. In our own service we have seen over 1800 patients and, as patient's needs and conditions change over time, we would need to review them to give an up-to-date clinical opinion and this would not be feasible with such a large number.	Thank you for your comment. The committee did not intend that every patient would need consultation from the specialist team. Instead it is required that the team are available to offer support when this has been identified by primary care.
Royal College of Occupational Therapists	Guideline	023	007	Whilst patients are under a specialist service, they should have a named contact within the team. However, this can't be sustained after discharge due to the number involved and practicalities of remaining up to date with people you are not in contact with, which would introduce risk. In our service we have a more prolonged period of contact with patients and patients can contact the service after discharge for advice/support but would need re-referral for further periods of intervention if needs have changed.	Thank you for your comment and this information. The committee agreed that a named contact (either in primary care or specialist care) was important for people with ME/CFS to navigate their access to care and reduce the burden of many appointments. See Evidence review I- multidisciplinary care for details of the committee discussion. The committee discussed discharge from services and some of the committee members described a similar experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.
Royal College of Occupational Therapists	Guideline	024		There no importance of assessing and retraining/addressing breath work / respiratory functioning for ME/CFS patients. This is a vital part of a treatment programme, how we breath has a significant impact on cellular functioning. (This is especially relevant currently when post Covid-19 virus patients are being seen despite the initial disclaimer that the evidence for post Covid patients has not been reviewed.) Energy envelope does not give adequate guidance of the many complex aspects of how the body uses energy moment by moment. Specialist individual activity plans that fit with an individual's values and gives some meaning and purpose is key. Our specialist service has for many years initially always	Thank you for your comment. This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and the assessment includes physical health and functioning. *Covid-19* At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19

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				encouraged an Stabilisation phase then as part of or following this the term "restorative" movement is encouraged. This can be in many forms (Stretches, walking, Qi gong, Tai Chi, Yoga, Pilates) that suit the individual. "Rest" is not a helpful term as people assume watching TV or just sitting is rest…it isn't. "Restorative" rest is key and many need help and guidance as to how to do this but its benefits are very well evidence based in other areas of clinical research. The new guidelines need to focus and put more in around gut health as significant numbers of people with ME/CFS have Gut Dysbiosis and need specialist dietetic support beyond what the standard NHS dietician service can often offer.	includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations. NICE are developing and updating the COVID-19 rapid guidelines in order to reflect that evidence. *Energy envelope* After considering the stakeholder comments the committee agreed to make some edits to the recommendation clarifying that it: • includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity. • uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse) *Rest* The committee agreed that rest was an important part of managing activity in people with ME/CFS. The role of rest and sleep are further addressed in section 1.12 and the rationale provides further information on this

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					Dietetic support The guideline highlights the importance of diet and nutrition and support throughout the recommendations, it is part of the initial assessment and there is a comprehensive section in the management of symptoms section. This is also reflected in the section on people with severe and very severe ME/CFS. There are clear recommendations when people with ME/CFS should be referred to dieticians with a special interest in ME/CFS.
Royal College of Occupational Therapists	Guideline	024	002	We think it is helpful to indicate how long this process can take and in some people it can take years, this is why we work with people over a prolonged period, for mild/moderates from 1-2 years and for our severe/very severe patients this is ongoing over many years. It would be helpful to have a further sentence to indicate that is can be influenced by numerous factors such as severity, co-morbidities, and situational context. Some services are only commissioned to provide 4-6 sessions which will not effectively help people with the process of implementing the advice and ensuring it is sustainable.	Thank you for your comment.
Royal College of Occupational Therapists	Guideline	024	004	Question 1: We are concerned that the statement implies that there is nothing that can be done to improve the symptoms and commissioners may take this nihilistic perspective as no health interventions need to be provided. We have consistent feedback from patients that they value the input from specialists, with expertise and knowledge, and many report positive changes and improvements in relation to strategies and approaches. We are concerned that the emphasis needs to be on individualised and client centred care that is monitored over time to ensure that there are no negative effects to any changes. It is important to support patients through relapses and ensure that they are able	Thank you for your comment. The committee agree that care for people with ME/CFS should be individualised with regular review and support through relapses. This is all recommended in the guideline. To note that after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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				to sustain changes, rather than short courses over limited time periods and discharge patients before they can successfully maintain stabilisation.	
Royal College of Occupational Therapists	Guideline	024	010	We feel that the initial statement that this is 'not curative' implies to people that these strategies have no benefit and it would be more helpful to put this as a positive that it is about trying to stabilise and improve the symptoms and coping with the condition, which still does not imply it is a cure.	Thank you for your comment. The committee agreed to keep, 'is not curative' at the beginning of the recommendation. In the rationale for managing ME/CFS the committee outline **why** it is important that it is clear there are not any cures for ME/CFS.
Royal College of Occupational Therapists	Guideline	024	011	It is important to recognise the expertise required from the health professional, not just support, in order to analyse and give expert advice on activity modification in relation to energy and activity that is assessed as appropriate to the individual's variability. These are core skills of occupational therapists and not core skills of other professional groups.	Thank you for your comment. The role of occupational therapists in supporting people with ME/CFS are acknowledged in the guideline and particular with reference to supporting people with ME/CFS who have difficulties caused by reduced physical activity or mobility or feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise programme into managing their ME/CFS.
Royal College of Occupational Therapists	Guideline	024	013	It is important to specify here that activity includes physical, cognitive, and social activities, including the environmental context and emotional impact of the activity on the individual rather than have it in a link as it common for people to misinterpret the concept of activity.	Thank you for your comment. This has been edited to.' includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity'.
Royal College of Occupational Therapists	Guideline	024	013	We are concerned that the list only refers to demands on energy, such as activity and focuses on how energy is used. Effective energy management also considers supply of energy. The concept of a seesaw balancing supply and demand of energy is often used to reflect the homeostatic processes that occur within the body to constantly attain equilibrium. This is why energy management requires constant adjustment to a wide range of factors that affect homeostasis, such as temperature, energy resources from food, hydration, light, hormonal changes, infection, metabolism changes, and other internal and external demands. So, it is important to include aspects of supply in energy management, such as sleep, nutrition, fluid, relaxation,	Thank you for your comment. This has been edited to.' includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity'.

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				breathing patterns, heart rate, and enjoyment/pleasure. An example would be that many people are unaware of the role of light in regulating the internal hormonal rhythms, and some due to light sensitivity may be restricting light.	
Royal College of Occupational Therapists	Guideline	024	014	In addition to understanding the energy envelope, people often need help with identifying this in practice as it can be easier to understand the principle than to identify actual levels. This needs to be linked to the concept of minimising fluctuations in symptoms, reducing post exertional malaise and therefore achieving greater stability in symptoms.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits'.
Royal College of Occupational Therapists	Guideline	024	016	This should reflect the need to learn to judge where the limits are and not assume that people know where they are. The commonest problem we encounter is that people will push themselves or over increase activity on the days their symptoms are less, increasing the post exertional reaction. A key component is enabling people to stabilise so they can sustain activity over time and reduce the boom and crash pattern.	Thank you for your comment. The committee agree and the next bullet point includes help from a healthcare professional to recognise when they are approaching their limit (children and young people in particular may find it harder to judge their limits and can overreach them)
Royal College of Occupational Therapists	Guideline	024	018	This is not specific to children and young people, we find adults are often driven by responsibilities and guilt to exceed their limits, even when they know they should stop.	Thank you for your comment
Royal College of Occupational Therapists	Guideline	024	022	We agree with the concept that this is tailored, flexible and is never automatic. However, we are concerned that the wording that you increase activity when symptoms decrease may lead to people over increasing on better days rather than being on a stable, sustainable baseline. We use the concept of achieving stability as the first stage and then making very small increases which still maintain stability, then sustaining this before the patient decides to make any further increases. In our experience patients tend to overestimate how much they can increase which causes destabilisation. We often use a guideline of around 10% - 20% of sustainable activity whereas, people will often double levels, such as increasing from a 5 minute to a 10 minute walk, so 100% increase. The general approach is that the sustainable	Thank you for your comment and information. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse)'.

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				baseline should be achievable five days out of seven as there will be days when patients' symptoms increase and they, therefore, should decrease their activities and rest accordingly. If it is not sustainable, then the level itself may need reducing.	
Royal College of Occupational Therapists	Guideline	025	003	Question 3: We agree with this statement and believe that a dysregulation model that encompasses the range of systems affected, such as autonomic nervous system, immune and endocrine function is more helpful and provides a better rational for the approaches of energy management, stabilisation and very gradual change where appropriate. In our service we differentiate between stages of stabilisation and then increasing tolerance so that it is clear to patients not to focus on increasing any activity until or if they have achieved improved stabilised/ reduced variability.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context
Royal College of Occupational Therapists	Guideline	025	004	This also needs to include environmental factors, such as housing, support, and finances. Also occupations, such as work, education and leisure. We would expand activities of daily living to include 'and personal care activities'.	Thank you for your comment. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The area you mention is included within the topics included in overview. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.
Royal College of Occupational Therapists	Guideline	025	015	We are concerned that the statement implies that the professional establishes the pattern however this has to be a collaborative process and needs to be verified and modified over time as it can change, so is an ongoing process and is why constructive therapeutic input cannot be achieved in only a few sessions. This is part of enabling and empowering people to have the skills to stabilise and manage their energy longer term.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that

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					they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Royal College of Occupational Therapists	Guideline	025	016	We are concerned that the use of the word 'minimises' symptoms can be misleading. Initially stabilisation focuses on reducing the post exertional exacerbations, but patients are still likely to experience some symptoms at this point as the symptoms are persistent, but the focus is on not making them worse/reducing PEM. Otherwise, people may have an expectation that stability means that symptoms are minimal and will see it as failure if this isn't achieved whereas it is about reducing variability initially and then gradual improvement, if possible, in symptom levels over time.	
Royal College of Occupational Therapists	Guideline	025	018	For some people it may be about reducing activity levels whilst for others it may be about spreading the same activity over a different time frame to prevent exceeding tolerance levels, for example staying with the anaerobic threshold by doing a task for shorter durations and allowing recovery time.	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
Royal College of Occupational Therapists	Guideline	025	019	Question 3: We are concerned that a stronger emphasis needs to be included on improving the quality of rest. Many people perceive that rest is the absence of physical movement, however it is important to activate the parasympathetic response that supports restoration. Therefore, learning how to relax and reducing use of cognitive and social activities during rest can support increased quality. In our service we find it helpful to go through the physiology of the sympathetic and parasympathetic systems to enable people to have greater understanding with how restorative biology works and why they need to work on the skill of rest. It can be helpful to use heart rate monitoring with some people to reduce their heart rate at rest, if this is high, prior	Thank you for your comment. The committee agreed that rest was an important part of managing activity in people with ME/CFS. The role of rest and sleep are further addressed in section 1.12 and the rationale provides further information on this.

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				to increasing any exertion.	
Royal College of Occupational Therapists	Guideline	025	022	The periods of activity need to be assessed against the individual's tolerance levels for each activity, so for example someone may be able to manage 10 minutes of cognitive activity but only five minutes of physical. Also, that it is better to subdivide an activity into shorter periods at higher frequency, so for example instead of 30 minutes on a task, doing three ten minutes through the day. Some therapy programmes give prescribed durations for activity, for example all activities will be 15 minutes, but this does not account for the individual variation between types of activity and context.	Thank you for your comment. The recommendation is to work with the person to establish an individual activity pattern and these bullet points are examples of what might be useful.
Royal College of Occupational Therapists	Guideline	025	023	It is important to recognise that no energy plan should be fixed, people and their condition vary, and the skill is to learn how to adjust and modify this. As people's symptoms improve or get worse there needs to be means to adapt the plan to suit.	Thank you for your comment. The committee agree and the recommendations are to work with the person to establish an individual activity pattern and for it be reviewed according to the person's circumstances.
Royal College of Occupational Therapists	Guideline	025	027	Some people may already use tools, but they can also be suggested for patients who have not tried these.	Thank you for your comment. There was a lack of effectiveness evidence on tools to support recommending people to monitor activity management. However, the committee considered the qualitative evidence (Evidence review G-Non pharmacological management) and their experience about the benefits of people using tools to monitor activity alongside the potential harms of increasing their burden and causing anxiety about activity levels. On balance the committee agreed it was important that self-monitoring of activity was acknowledged and where used it should be as easy as possible.
Royal College of Occupational Therapists	Guideline	026	004 - 005	This can include any activity not just physical activity. To increase occupational activity or the demands of those occupations. Both physical and cognitive demands.	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice

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					on maintaining and preventing the deterioration of physical functioning and mobility.
Royal College of Occupational Therapists	Guideline	026	001	Question 1: We disagree with the statement that patients should only be referred to an Occupational Therapist in relation to physical activity. Occupational Therapists are trained and qualified in all areas of activity analysis and management. The restricted focus on physical activity devalues the role of cognitive, social, quality rest and emotional activities in people's lives and the benefit of providing intervention across all these areas to improve quality of life. You can't isolate one type of activity, such as physical, without considering all the other activities people are engaged with at the same time. Occupational Therapists have an important role in helping people stabilise symptoms, not just in increasing activity levels. They have key skills in energy management which is applicable to all patients. Why would this be restricted to patients who have long term symptoms or severe illness when early intervention and expertise could improve symptoms or prevent deterioration as stated previously in the guideline? It should be clearly stated that referral for specialist occupational therapy would be for any type of activity, for help with management or progression. Occupational therapists will be key professionals in doing the assessment for, and delivery of, the management plan discussed previously. If Occupational Therapists aren't delivering the energy management plans which require specialist skills in activity analysis and adaptation, then who will be delivering these and are they qualified to do so?	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The role of occupational therapists in supporting people with ME/CFS are acknowledged in the guideline as part of the ME/CFS specialist team. Here they are directly named with reference to their training and expertise in supporting people with ME/CFS who have difficulties caused by reduced physical activity or mobility or feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise programme into managing their ME/CFS.
Royal College of	Guideline	026	012	From our work with severely and very severely affected it is even more important to have a prolonged assessment period as they are likely to have complex needs and co-morbidities. To then	Thank you for your comment.

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Occupational Therapists				focus on stability prior to any consideration of increases within energy management. It can take considerable time just to stabilise their care package so that any care being delivered has a minimised impact on their health. So, factors such as the environment, nutritional intake and fluid, contact times, sensory sensitivities, sleep quality and pain reduction may need to be stabilised first. Due to orthostatic intolerance this needs to be addressed, such as though working on positioning using a profiling bed or electric recliner chair, prior to increasing activity levels. Often our role is in multiagency working to ensure other professionals and carers understand the illness and recognise that individuals very specific needs and intolerances.	The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging The committee agree that some people may need more than one assessment or different approaches to assessments and developing the person's care and support plan.
Royal College of Occupational Therapists	Guideline	026	017	The needs for physical maintenance within the management plan will vary dependant on the severity of the condition and should be recognised that it is likely to be more involved for someone who is severely/very severely affected. For someone with mild to moderate illness, it is important to include orthostatic tolerance on this list. Many people are not aware that lying down for prolonged periods will reduce this and that it is important to rest in different supported positions, to gradually increase time being challenged by gravity, such as foot to floor time, and to vary positions. Related to this is whether fluid intake should be included as again people can often not be aware of the impact of reduced blood volume. Some patients who have improved their orthostatic tolerance through sit to stand training found this helpful. Also, people need to aware of the importance of weight bearing and looking at alternative ways to achieve this when a patient isn't mobile. It is also important to mention dental health as patients can develop problems with their teeth and can struggle with maintaining dental hygiene.	Thank you for your comment. After considering the stakeholder comments, 'Include strategies to maintain and prevent deterioration of physical functioning and mobility in the care and support plans for people with ME/CFS. Strategies may need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the care and support plan and the priorities and symptoms that people may have. Dental health has been added into recommendation 1.10.1 to highlight its importance.

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				Another problem in younger patients who are still growing is the impact of poor positioning and constant bedrest without regular postural changes and adequate support on spinal development and we have patients who have required later surgery for scoliosis. Should it also be mentioned in this section about monitoring of vitamin D due to lack of exposure to sunlight.	
Royal College of Occupational Therapists	Guideline	027	014	Question 1: There is an assumption here that aids and equipment will always be of benefit whereas for some patients, there are risks. Provision of walking aids, such as a walking stick may help balance, but may encourage people to walk further than their tolerance level or increase fatigue levels due to having to carry the stick or poor posture through leaning to one side. There can also be an assumption that now they have the equipment they can complete the task which may not be true. So, for example some of the patients we work with who were given stair lifts found that the exertion required to get on and off, tolerate the movement and sit upright increased their PEM, as did being in a less restful environment when they got downstairs. They preferred to have a day area upstairs and only use the lift when they felt they have greater capacity to do so. So, the provision of equipment doesn't necessarily eliminate the problems and it needs to be understood that they are tools and don't necessarily improve the individual's functional abilities. If there is going to be increased provision of equipment it needs to be considered how these should be used and how they will integrate with the broader management plan.	Thank you for your comment. The committee disagree this is assumption here about aids and equipment. This is a list of examples families and carers may need advice on. In the section on aids and adaptions recommendation 1.8.8 includes that the risks and benefits of aids and adaptions should be considered.
Royal College of Occupational Therapists	Guideline	027	023	It is important to reinforce this in relation to known biological changes in ME/CFS, such as the alteration of the anaerobic threshold and the impact of cumulative exertion as demonstrated in research on repeated exercise testing. Health professionals may not be aware of this factor and it is important that it is explicit	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. The point you make is discussed further in committee discussion

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				so that patients are not encouraged to undertake cardiac exercise.	in evidence review G and for this reason your suggestion has not been added to the recommendation.
Royal College of Occupational Therapists	Guideline	028		It is positive that the importance of early diagnosis and of being believed has been highlighted since this will contribute to early assistance being offered, which in turn will stop sufferers being unfairly labelled or stigmatised plus will facilitate early intervention which in turn will enable a swifter return to better health and wellbeing. If greater emphasis could be placed on this then it would assist the guidelines being more positively focused. Similarly reversing statements such as "tell people about the risks and benefits..."p 28 would help by putting the positives before the negatives. Also, the encouraging nature of the research which is currently underway could be emphasised, rather than the limited nature of the currently published trials which implies a lack of confidence in what is currently achieving good results.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.).
Royal College of Occupational Therapists	Guideline	028	001	Question 1: We understand the need to exclude fixed exercise programmes but saying that patients should be excluded from any physical activity as a treatment for symptoms of ME/CFS, may exclude orthostic treatments, such as recumbent exercises for POTS/orthostatic intolerance. Also, many patients choose to focus on goals in relation to physical activity, such as being able to walk further or play with their children. Physical movement and activity are part of everyday life for most people, particularly in the mild to moderate groups. Therefore, it is an important part of energy management to look at how to do physical activity differently, such as reducing standing, shorter durations, reducing heart rate, energy conservation techniques and achieving stability in these areas. If the PEM in response to this	Thank you for your comment. After considering the stakeholder comments the committee have edited this recommendation and 'derived from osteopathy' has been removed. The committee agree that there are people with ME/CF that may feel ready to progress their physical activity beyond their current activities of daily living and have included this in the reasons for referral to a physiotherapist or occupational therapist working in a ME/CFS specialist team to explore how to do this safely.

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				physical activity reduces people will naturally start to do more and it is important that they have the right information about how to do this within the anaerobic threshold and still maintain stability. Limiting intervention to only when people are ready to progress ignores the work that needs to be done to stabilise current physical activity first.	
Royal College of Occupational Therapists	Guideline	028	008	It is also important to acknowledge that although deconditioning is not the cause of ME/CFS for some people it will become a secondary factor due to prolonged disability.	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise intolerance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation and replaced with 'perpetuating ME/CFS'.
Royal College of Occupational Therapists	Guideline	028	023	We are concerned that a physical activity programme should not be designed without consideration of the overall pattern of activity, including other types of activity. If you focus on one aspect in isolation, you are not considering the other areas of demand. We would consider that this should be an integrated component of a complete activity management programme otherwise there are risks. For example, if the patient is focusing on increasing their walking but this then impacts on their ability afterwards to be with their children. Life is not undertaken in separate compartments.	Thank you for your comment. The committee agree that all of the person's activities should be considered when developing an energy management and if appropriate a physical activity plan.
Royal College of Occupational Therapists	Guideline	029	017	As stated previously it is important to clarify what is meant by rest and that this is a change in our physiological state and not just the absence of muscle movement. For some people certain activities can be restful. The key factor is whether the brain is in a	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS.

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				sympathetic or parasympathetic state. Many people describe that although they are physically resting, they find it difficult to switch off their thoughts, they remain in a high sympathetic state and some will have a high heart rate even when sitting. This section doesn't emphasis the important role that quality rest and relaxation have in regulating the autonomic nervous system and supporting functions of the parasympathetic nervous system, such as sleep, digestion, immune function, and energy production. Many people were used to being highly active and find it very difficult to engage in quality rest so this can be a key part of specialist intervention and needs to be addressed to gain stability before increasing exertion.	There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Royal College of Occupational Therapists	Guideline	030	003	Question 3: Managing orthostatic intolerance is a key component of specialist intervention. This section makes no reference to management techniques that can improve orthostatic tolerance, such as fluid intake, salt, use of compression, improving stabiliser muscles, changing positions, and recumbent non cardiac exercise to increase lower limb muscle tone. As this can be a key symptom then some aspects of management should be included under the role of specialist services, for example some people report that increasing their fluid intake reduced symptoms, such as dizziness.	Thank you for your comment. The committee did not make any recommendations on the management of orthostatic intolerance noting that although this can be straightforward it this can involve advice on diet, carrying out daily activities and activity support and should be tailored to the person taking into account their other ME/CFS symptoms. The committee noted medicines usually prescribed for OI can worsen other symptoms in people with ME/CFS and should only be prescribed or overseen by a clinician with expertise in orthostatic intolerance. (see evidence review G).
Royal College of Occupational Therapists	Guideline	032	008	Question 2: There are very few dieticians who specialise in ME/CFS, therefore, how is this need going to be met for any patients with nutritional needs or are severely affected without additional funding and training for specialist dietitians?	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better.

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Royal College of Occupational Therapists	Guideline	034	006	Question 1: Many services are not based on CBT/GET, and do not have access to psychologists or specialist CBT therapists e.g. in many areas, CBT is delivered through the IAPT services. They follow a psychosocial model and would still consider ME/CFS under medically unexplained conditions. As this guideline still states there is no pathology and makes no reference to any biological or physiological changes then this is still likely to be considered as a suitable pathway. So, either there needs to be funding for provision of specialist ME/CFS CBT therapists across the NHS or how will this specialist knowledge be integrated with existing generalist pathways and CBT services which exist under mental health. Occupational therapists use some aspects of CBT to help people with adapting and implementing changes to improve their health or being compassionate to themselves where they experience thoughts or believes that may be barriers to managing their health, such as 'I can't stop I have to get this done' or 'I will be letting people down'. We consider this as part of implementing activity management rather than thoughts are causing or perpetuating the illness.	Thank you for your comment. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed.
Royal College of Occupational Therapists	Guideline	034	030	The components listed under CBT are identical to those for all aspects of therapeutic intervention, why are they only specific to CBT and how is this different to energy management? The guideline seems to be describing the same intervention under two different names.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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					reviews G and H for the evidence and the committee discussion on these recommendations). CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness and if chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
Royal College of Occupational Therapists	Guideline	037	012	It can also be important again during a flare to reinforce the value of quality rest, such as using breathing and relaxation to help with restoration.	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available.
Royal College of Occupational Therapists	Guideline	038	008	Question 1: There is an assumption that a health professional in primary care will have the knowledge and expertise to advice someone with ME/CFS how to manage a relapse. Where are they going to get this knowledge and training from?	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. • To note the training recommendations have been edited.
Royal College of Occupational Therapists	Guideline	039	002	Question 1: as above how are primary care staff going to develop the specialist knowledge and expertise to review a management plan, including advising around energy management? How is the time for this going to be funded considering that more people will be getting the diagnosis? The majority of our patients only consult their GP in relation to medication as the GP does not have the same understanding of their condition as they do. Are we expecting GPs to develop skills in managing dysregulation, activity analysis, energy management, social care services and	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. People getting the diagnosis We do not agree that more people would necessarily get an ME/CFS diagnosis. The diagnostic criteria are slightly stricter

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				aids and equipment when they do not cover these areas for any other health condition?	than in the previous guideline. Reflecting on stakeholder comments, the committee have removed reference to a provisional diagnosis from the recommendations. Support for GPs The committee have recommended that GPs can approach the ME/CFS specialist team for advice about referral and care. Implementation and funding The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.
Royal College of Occupational Therapists	Guideline	039	003	Question 3: Annual review appointments are often not popular with people due to the fluctuating nature of the condition. For example, if patients had improved then they may cancel due to other commitments such as work or school, those who were too unwell at that point would cancel as they felt it would be detrimental to have the demand of an appointment at that time. Also, some patients may be doing well at that point then relapse afterwards or have already relapsed and being doing better by time of the appointment. It is often more successful to offer advice or support at the patients request when they feel they need it, usually by email or telephone call, as this is more accessible and is less wasteful of clinical time in cancelled appointments.	Thank you for your comment. The committee agree that the need for an annual review will depend on the person's circumstances. Some people may not need an annual review for various reasons, including involvement of secondary care services, or will decline a review but the committee agreed it was important that people with ME/CFS were offered the opportunity to have care related to their ME/CFS reviewed at least once a year in line with other long term conditions. In addition the committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as

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					online communications may be more appropriate depending on the person's symptoms. The committee note that the review here is based in primary care and this would reduce the need for travelling to specialist centres.
Royal College of Occupational Therapists	Guideline	039	021	It should not be assumed that all new symptoms are related to ME/CFS and referred to specialist services. Each new symptom is investigated in its own right to ensure the patient hasn't developed other health conditions and not just dismissed as part of the ME/CFS spectrum.	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline.
Royal College of Occupational Therapists	Guideline	040	012	Question 2: Some services provide training to GPs, AHPs and medical students. However, to provide this on the scale required to ensure that every practitioner across hospital, community and social care services who may come into contact with someone with ME has the appropriate training would require significant investment in large scale training. Although there are online training courses available which can increase awareness this does not necessarily give professionals the expertise and confidence to deal with this complex condition in practice. This guideline places considerable responsibility on primary care to assess this condition, devise and review management plans and provide support for relapses which requires more than a one-off training session and underestimates the complexity and diversity of this patient group,	Thank you for your comment. The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be considered by NICE where relevant support activity is being planned.

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Royal College of Occupational Therapists	Guideline	071		Reversal of CFS/ME (used by most services currently) to ME/CFS will be very expensive for all services to reprint their literature especially when the term ME is clearly not fully supported within the NICE guidelines.	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
Royal College of Occupational Therapists	Guidelines	General	General	We are concerned that there is limited reference to the skills and expertise of occupational therapists except in restricted functions, such as intervention for physical activity with those with long term symptoms. As occupational therapists are specifically trained in the occupational performance disruption, adaptation and participation, analysis of activity of all types, client-centred approaches and supporting people in engaging in activity alongside health needs, occupational therapy should be offered to everyone with ME/CFS. This will enable them to support people in energy management, approaches to activity to support health, enable support for people in work, education and training, and appropriate rehabilitation, as necessary. Occupational therapists have an in-depth understanding of occupational identities and roles and can support people in finding alternative approaches and modification of activities in order to enable engagement in activities that offer a sense of meaning and purpose, a sense of identity, and notwithstanding disability enable productivity. This occupational therapy intervention is delivered whilst working within the principles of an envelope of	Thank you for your comment. The committee agree that the skills and expertise of occupational therapists are important in the management of people with ME/CFS. Where the specific expertise of an occupational therapist is required this is directly recommended.

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				energy with a focus on stabilising and then, when appropriate, increasing activity within tolerance levels due to expertise in activity analysis. There is an assumption through the guideline that any health professional is qualified and trained in these skills which we feel needs to be challenged.	
Royal College of Occupational Therapists	Guidelines	General	General	The draft guidelines are somewhat pessimistic in tone "Only a small proportion recover", p 14; " it is less common to have long periods of remission" p14 "there is no treatment or cure" p24 .... The guidance does not indicate adequately the many positives of what can usefully be done to improve health and wellbeing. Specialist teams have been running now for over 15 years and this is NOT what is commonly seen in practice. Practice based evidence needs to be taken in to account. There is a great deal of expertise in specialist teams and many clinicians do not and never based their therapy approach purely on CBT and GET. Many patients feel robbed of control when experiencing symptoms, plus have lost self-confidence, often have had to cease work and social activities et cetera and are feeling low in mood. A belief that there are things they can do to restore their health and well-being is very important and current guidelines do not capture this or that services are getting very positive results, with some patients regaining excellent levels of functioning as indicated by many patient evaluations received following our person centred treatment programmes. A newly diagnosed young person or adult would feel very concerned about their long term future if at diagnosis they heard there was "no cure" and "no treatment" this would perpetuate vicious cycles. There are many clinical studies looking at the Nocebo effect in a whole range of conditions. Hope is an intrinsic part of how humans respond to disease. Just because research studies thus far have	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. *Treatment or cure*

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				demonstrated why the guidelines might put this in our specialist view this reflects more on how the research was done than how we see day to day our patients respond in practice. Whilst all services are constantly developing and improving which enhances their efficacy, assisted by the research results being published; no rehabilitation will be 100% effective for all sufferers especially when a condition is so multifactorial and complex as ME/CFS, the studies that have demonstrated positive therapeutic results do not come through in the draft. Inevitably as ME/CFS is "an umbrella label" encompassing many disturbances in homeostatic mechanisms, it will not be straightforward to research until subdivisions/subtypes of what is awry are further defined. Highlighting this too would assist people in understanding why research will take time as currently research groups tend to be very heterogenious so clear findings tend to be diluted. Whilst the complexity of the condition needs highlighting which does come through well in the guidelines, they need to facilitate for patient readers some hope and optimism including encouraging them to form a partnership with the services who are able to help them. With this complex condition, it is not just the techniques that are important but the context of these i.e. the formation of a trusted alliance with a therapist/service which reduces the isolation and responsibility from the patient to find out what to do themselves that is important. There is a lot of focus on physical activity and exercise and possibly not enough on cognitive activity as this can often be	After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.

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				more fatiguing. People also often need education and information on this.	
Royal College of Occupational Therapists	Guidelines	002		Question 1: It is stated that the recommendations in the guidelines should not be assumed to apply to people who have fatigue after COVID-19, however by the definition given of suspected or diagnosed ME/CFS a very high proportion with Long-Covid or Post-Covid Syndrome would meet criteria for a ME/CFS diagnosis, and therefore, whilst the evidence for the guideline was considered by the committee prior to the pandemic, consideration for inclusion of this group of people should be made in the guideline.	Thank you for your comment. At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations. NICE are developing and updating the COVID-19 rapid guidelines in order to reflect that evidence.
Royal College of Occupational Therapists	Guidelines	008	008	Further detail is required to indicate what is being considered in a psychological wellbeing assessment - considering mental health or psychological wellbeing stressors or factors that could be contributing to the presenting symptoms. It is a factor that is regularly under-estimated on referral to specialist clinics.	Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments carried out when a person visits a clinician with an undiagnosed illness. This part of the assessment is to capture how the person's symptoms are impacting on their lives and how they are feeling. To capture this better psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
Royal College of Paediatrics and Child Health	Guideline	General	General	Children are not mini adults, they present with CFS/ME differently, respond differently to treatment and recover in different ways too.	Thank you for your comment. The committee agree that children are not mini adults. Children and young people are named as a group for special

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					consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	There is a lot of concern about the evidence base which the updated draft guideline is based on as it mostly focuses on adults. Some trials have been excluded which reviewers have recommend are included, there is intrinsic bias and some evidence seems to have been self-selected and qualitative and survey data from patient groups has been included which must be interrogated further.	Thank you for your comment. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Trials excluded* No evidence has been excluded that met the inclusion criteria in the protocols. See the methods chapter for more information on GRADE and indirectness. *Qualitative data and relevance* After considering the stakeholder comments the committee agreed to revisit the qualitative evidence for the experience of interventions further scrutinising the information on PEM reported in the trials and the application of relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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Royal College of Paediatrics and Child Health	Guideline	General	General	As far as the reviewers are aware, NICE appear to have not engaged or consulted with anyone who runs a paediatric CFS/ME service.	Thank you for your comment. The committee included members working with children and young people with ME/CFS within a ME/CFS paediatric service. To note children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	There is very little focus on children and young people who have mild to moderate symptoms/condition. The guideline almost entirely focusses on severe diagnoses.	Thank you for your comment. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to develop recommendations that were individualised but reflected the variation in the impact and severity of symptoms that people with ME/CFS experience. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and these recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
Royal College of Paediatrics	Guideline	General	General	The tone of the guideline is negative, with a number of points where the negative outcome is listed first. No numbers are given	Thank you for your comment.

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and Child Health				alongside this, so it creates an impression of consistently poor outcomes.	When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to develop recommendations that were individualised but reflected the variation in the impact and severity of symptoms that people with ME/CFS experience. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
Royal College of Paediatrics and Child Health	Guideline	General	General	It appears that there has been no engagement or consultation from practices that provide a paediatric service for CFS/ME in the NHS in this guidance.	Thank you for your comment. The committee included members working with children and young people with ME/CFS within a ME/CFS paediatric service. To note children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	This guideline assumes the same for adults and children, however their experience, presentation and treatment can be very different. Children and young people are not "small adults", the presentation, time course and evidence around treatment are all different to the adult experience and that is not clearly reflected in the draft guidance.	Thank you for your comment. The committee agree that children are not mini adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.

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Royal College of Paediatrics and Child Health	Guideline	General	General	Whilst it has been noted that "parents may act as an advocate" there should be and exploration of the role of independent advocacy to support children and young people through their patient journey with ME/CFS rather than a reliance on parents/carers to take this role.	Thank you for your comment. After considering the range of stakeholder comments on advocacy the committee agreed to add, 'recognising that a child or young person may need to be seen on more than one occasion to gain trust, (this may be with or without their parents or carers or without, as appropriate) to the section on additional principles of care for children and young people with ME/CFS. The definition of advocacy in the guideline includes family members, carers, friends or an independent advocate.
Royal College of Paediatrics and Child Health	Guideline	General	General	Compared to the 2007 guidance, there is more information on children and young people, however, it is not specific to children and often not appropriate. In the evidence base there are only three papers cited that specifically look at children and young people; the total number of subjects in those studies was 26, with none aged younger than 12 years. Two of the studies were from single centres/services. One would expect the data on which these recommendations are based to be more robust.	Thank you for your comment. The committee agree that children are not mini adults. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate using their expertise and experience. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	The guideline appears to be based on a study involving a very small number of participants/families (16 young people who were recruited by Action for ME). This is a very biased small sample of young people who hadn't had access to specialist services and appeared were dissatisfied with their outcomes. It was questioned whether young people who had been successfully rehabilitated by existing specialist services were contacted to give feedback prior to revising the guidelines? The reviewers service keeps a proforma of patients with outcome measures and has good success rates from following the current 2007 guideline.	Thank you for your comment and information. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations.

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				The reviewer's concern would be that by radically changing the current guidelines it will be found that their service will be difficult to deliver as they use a combination of GET, CBT and activity management to good success currently. The families are often complex, and they are able to encourage engagement with the support of the current guideline. The reviewer believes that their service is an example of good practice and has excellent success rates whilst in line with current guidelines. The overall draft guideline seems to support more regional access to specialist services which is positive, but this would need a lot of increased funding to make this available nationally. If not, it could put pressure on existing services if asked to cover a larger area. Areas having the biggest impact would be abolishing the guidelines to include GET, CBT and activity management. The guideline states that these should no longer be used and that patients should be advised to stay within their energy envelope and only be offered CBT to support their mental wellbeing, not as an active part of rehabilitation. If the reviewer didn't have the robust, evidence-based support from NICE to continue their therapy in their current, highly successful service they would find it impossible to make progress with many of their complex young persons.	One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As you note one of these was on children and young people. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). In addition children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate using their expertise and experience. Where this was the case separate recommendations were made.

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					Appendix 1_Children and Young people. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and the representation of the sample. *Funding of services* The guideline reflects the evidence for best practice and highlights areas where resources should be focussed. There are areas that may need commissioning and investment, such as access to specialist teams, to implement some recommendations in the guideline. *Physical activity* After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a

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					ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
Royal College of Paediatrics and Child Health	Guideline	General	General	The guidance says a number of times that there is no treatment and no cure, but then goes on to list a number of things professionals should either do or offer. If these are not treatments, then what are they? Some clarification is required. The reviewer would argue that if something (like CBT) is offered to improve wellbeing and mood and other aspects of life, and may improve these areas, then that is a form of treatment.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations and to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Royal College of Paediatrics and Child Health	Guideline	General	General	There appears to be a lack of information regarding treatment in children and young people. The question "what does success in the treatment of this population look like" needs to be asked. The focus on "the lived experience" neglects the effects (positive and negative) of interventions; there is also the possibility that those who have experienced successful interventions will have left	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations and to avoid

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				follow-up and hence do not contribute to the assessment of "the lived experience".	any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate using their expertise and experience. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	There is a lack of information on mild/moderate severity of CFS, especially in relation to transition, patients that transition from children to adult services might be mild to moderately affected by CFS.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to develop recommendations that were individualised but reflected the variation in the impact and severity of symptoms that people with ME/CFS experience. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). The NICE guideline on transition from children's to adults' services is cross-referred to in the guideline and has more information on the general principles of transition.
Royal College of Paediatrics and Child Health	Guideline	General	General	It has been found that a lot of qualitative papers have been excluded in this review. Please see references below that highlight recent papers on children and how they differ to adults with CFS/ME. A lot of the relevant evidence was downgraded or	Thank you for your comment. Any studies that met the inclusion criteria for the protocols have been included in the evidence reviews.

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				excluded. In particular, there is concern that given the limited age range covered by the three papers currently used as the basis for the recommendations, the exclusion of papers that include younger children is detrimental. References - Brigden A, Shaw A, Anderson E, Crawley E. Chronic fatigue syndrome/myalgic encephalomyelitis in children aged 5 to 11 years: A qualitative study. Clinical Child Psychology and Psychiatry. October 2020. doi:10.1177/1359104520964528 - Loades, M.E., Read, R., Smith, L. et al. How common are depression and anxiety in adolescents with chronic fatigue syndrome (CFS) and how should we screen for these mental health co-morbidities? A clinical cohort study. Eur Child Adolesc Psychiatry (2020). https://doi.org/10.1007/s00787-020-01646-w Collin SM, Nuevo R, van de Putte EM et al Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) is different in children compared to in adults: a study of UK and Dutch clinical cohorts BMJ Open 2015;5:e008830. doi: 10.1136/bmjopen-2015-008830	We have included papers on children and young people across qualitative reviews. As set out in the methods inclusion of studies was halted once data saturation was reached; meaning that no new themes/ new information relevant to the review other than what was already included emerged from further studies. Brigden 2020 was published after the final reruns for the literature were completed in October 2020**.** However, the reviews includes earlier publications by the same authors conducted in a very similar or the same population. Similar findings to those reported in this paper have been captured by the qualitative reviews e.g. the need for social support, the complexity surrounding diagnosis, the fluctuation of symptoms, the difficulty of adapting to everyday life with ME/CFS and also to medical care strategies, potential issues that both children and their parents face when communicating the child's experience to health-care professionals (Evidence Review C). Loades & Collin studies are cross-sectional and do not meet any of the review protocols. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature, one focused on children and young people.
Royal College of Paediatrics and Child Health	Guideline	General	General	Whilst it is stated that bias will be assessed using the CASP qualitative checklist, reading the study descriptions there is a repetitive theme of study participants being self-selected or brought in through identification using non-blinded/non-random	Thank you for your comment. Qualitative studies are critically appraised using CASP and the quality of the evidence is assessed using CerQual. The bias you raise is accounted for and included in the evidence synthesis

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				processes that are more likely to lead to bias and less likely to be properly representative of the population.	(see Evidence reviews G and H_ non pharmacological management). *Qualitative data and relevance* After considering the stakeholder comments the committee agreed to revisit the qualitative evidence for the experience of interventions further scrutinising the information on PEM reported in the trials and the application of relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal College of Paediatrics and Child Health	Guideline	General	General	The committee regularly say in its reasons for recommendations that the evidence is poor and therefore the recommendation is based on the committee's experience and knowledge. There are eight members of the committee who have CFS mentioned in their job role or committee role and five lay members. This is not a large number of people to base a consensus on and appears contradictory to the evidence reviews and discussions of bias elsewhere in the supporting documents. The reviewer noted that these recommendations that are not based on objective evidence are made clearer.	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but can affect the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline.

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					The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As you note one of these was on children and young people. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
Royal College of Paediatrics and Child Health	Guideline	General	General	As the evidence reviews are causing some difficulties (around studies that have been discounted etc.) the reviewer suggested that the recommendations for research be more explicit in asking for research that has more blinding, or looking for methodologies	Thank you for your comment. The committee agree that this should be clear in any research and have included this in the research recommendations. *Discounted studies*

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				that would reduce the subjective bias that is the cause of such concern (completely understandably).	No evidence has been excluded that met the inclusion criteria in the protocols. See the methods chapter for more information on GRADE and indirectness.
Royal College of Paediatrics and Child Health	Guideline	General	General	In the inclusion/exclusion criteria it is noted that studies were excluded where post-exercise fatigue duration was not stated; however, on review by study authors, in respect of the subjects in those studies with children and young people, they all met this criterion.	Thank you for your comment. After considering the stakeholder comments on the PEM the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the quantitative evidence and relevance in the qualitative evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct or relevant. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
Royal College of Paediatrics and Child Health	Guideline	General	General	The reviewer noted a systematic review on recovery in children (which is currently under review with the ADC) that shows a greatly improved recovery rate in children in comparison to adults.	Thank you for your comment and information.
Royal College of Paediatrics and Child Health	Guideline	General	General	There is a lack of data relating to children and young people, there are only three studies that reflect children and young people's direct experience; one more study related to the experience of those treating children and young people; and there is a statement that "the committee agreed evidence from the adult population reflected their knowledge and experience about children and young people and could be used to support their decision-making for children and young people". This is not an acceptable approach; there are a multitude of examples of the inappropriate application of adult approaches to managing childhood illness. This is an opportunity to have a set of children and young people specific recommendations for this debilitating condition that could and should be taken.	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As you note one of these reports focused on children and young people. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made.
Royal College of Paediatrics and Child Health	Guideline	General	General	It was noted that information from the national outcome database has not been used.	Thank you for your comment and information.
Royal College of Paediatrics and Child Health	Guideline	General	General	There should be reference made to the United Nations Convention on the Rights of the Child, specifically article 12, 23, 24, 28 and 31 which have been identified by RCPCH &Us children and young people with long term conditions / health	Thank you for your comment. The United Nations Convention on the Rights of the Child is not routinely referenced in NICE guideline. Although we note the

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				experiences as being important within their health. More details at www.rcpch.ac.uk/rightsmatter.	recommendations are in line with the UNCRC and in particular the articles you reference.
Royal College of Paediatrics and Child Health	Guideline	General	General	Even though the prevalence is found to be between 0.2 to 0.4% it is difficult to estimate the accurate prevalence due to a number of factors including lack of specific diagnostic tests, multiple case definitions, different methodologies and confusion about coding. Though the medical community is more informed than CFS/ME than previously, debate continues on the cause, diagnosis, pathology, physiology and treatment. Difficulties could also arise because of the quality of care patients could expect while recognising the public health objectives of equity, fairness and efficiency. All these factors will have a big impact on practice and will be challenging for the guidelines to be implemented. Good care depends on physical capacity, attention to details and skill built on experience. The fact that clinical practice guidelines relate more directly to the processes of care than to outcome by itself would be a challenge. The following should be considered; decreasing variability, ensuring that the voice of the child be heard, preventing under use of necessary care and overuse of unnecessary and inappropriate care, transition of care and recognising and responding to the complex symptoms of this condition. Striving for continuous improvement in context to the present goals would help achieve good implementation.	Thank you for your comment and information. The committee agree with points about the challenges of diagnosing and then supporting people with ME/CFS.
Royal College of Paediatrics and Child Health	Guideline	General	General	Decisions to recommend interventions should not be based on evidence of their costs and benefits alone. An indication of the effectiveness of a clinical guideline is the relationship between the medical benefits gained and the costs of achieving those benefits when the guideline is implemented. Sufficient time should be allotted to study in detail the economic analysis in relation to the implementation of a guideline in order to lessen the potential impacts of cost. The following should be considered to understand that costs and savings would play a direct impact in implementing these guidelines:	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences.

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				- In a 2014 survey, more than half (54% of patients with CFS) had not attended an NHS CFS clinic in the past five years (action for ME 2104) Create more professional and public awareness, consider the personal and social impact of the disease, flair ups and triggers and how to overcome these blocks to progress. To identify the price and cost of therapeutic interventions, pharmacological interventions, dietary interventions and use a costing tool that is consistent.	When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As you note one of these was on children and young people. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The NICE implementation team are assessing the resource impact of recommendations. We acknowledge that there is likely to be an increase in specialist resources required in some parts of the country in order to make the provision of care more equitable than it has been in the past. Commissioners will decide how best to implement this locally. We note that the recommendations do not emphasise continued involvement by the specialist team. Instead, the focus is on an initial assessment and management plan by the team. Follow up should continue to take place by the general primary care team.
Royal College of Paediatrics and Child Health	Guideline	004 - 005	004	1.1.1/ 1.1.6/ 1.7.2 - The reviewer accepts the features used in diagnosis and the statements about difficulties and fears of prejudice, however, it was felt that 'prejudice' should be followed by 'however, …. as in most complex paediatrics, children should be considered in their context of environmental and family	Thank you for your comment. The committee agree that when caring for children they should be considered in the context of their environment and families. The recommendations emphasise taking a child centered approach and developing a personalised care and support plan.

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				factors.' This also applies in the later safeguarding specific section 1.7.2.	These acknowledge that each child and their situation is different and this should be take into account. To ensure that each child or young person is assessed by a professional with training in paediatrics, the guideline recommends referral to a paediatrician when ME/CFS is suspected and then to a paediatric ME/CFS specialist team to confirm the diagnosis. Where safeguarding assessments are needed these should directly involve a paediatrician with training and expertise in ME/CFS.
Royal College of Paediatrics and Child Health	Guideline	004 - 005	004	1.1.1/1.1.6/1.7.2 - The sub section regarding the lack of evidence base that the team found for specific safeguarding issues is not evidence that there is none. The reviewer explained personal experience of several individual situations in which widely discrepant information not explained by fluctuations in symptoms etc. were drawn together from multiple professionals. These questions about the diagnosis and the management did not originate with the reviewer and came in the context of a local large case number specialist clinical service for CFS. It was noted that the reviewer can share these, but they are histories and case series and are difficult to write up. The cases are multi professional observations and evidenced with constructive detailed diagnostic independent specialist CFS clinical assessments, special interest and management, DLA criminal outcome and aspects of Case Reviews. The reviewer noted that they accept and understand the range and potential impact of this condition but feel there is a strong sense of bias in this guideline document and a need for some degree of change in the balance to be considered.	Thank you for your comment and information. The committee agree and the rationale linked to safeguarding notes that no evidence was identified. The committee membership includes members that have experience of safeguarding processes in children with ME/CFS. The committee have taken into account the wide range of perspectives and comments from stakeholders and have made edits to the guideline and hope these address the concerns that stakeholders raised about the balance in the guideline. Safegaurding was discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed.

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					This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Royal College of Paediatrics and Child Health	Guideline	005	027	1.1.7 - The reviewer agreed with the child-centred approach which was felt to be essential. However, it was noted that there are different interpretations and approaches to this and some barriers. Implementation of this in these circumstances is not well laid out e.g. how to access the voice of the child; how to evaluate this; consider routinely the access of the child to their basic essential needs and how to assess this; the environment and perspectives; the symbiosis that can occur; longstanding evidence from safeguarding literature about the risks of losing sight of the child in complex situations and possible ways of maintaining that etc.	Thank you for your comment. The committee noted that the Royal College have developed the ' Being Me' resources, with input from children and young people, to aid their communication with health professionals and have referenced these in Evidence review C-access to care to support readers of the guideline.
Royal College of Paediatrics and Child Health	Guideline	006	003	There are safeguarding issues around communication (specifically page 6) regarding the parents being advocates and communicating for the child, this should have a caveat of making sure there is a way to hear the child's voice without it always being through the parents.	Thank you for your comment. After considering stakeholder comments this recommendation has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity.
Royal College of Paediatrics and Child Health	Guideline	007	001	The guideline recommends that persons with severe or very severe ME/CFS may "need a low-stimulus environment, for example a dark quiet room with interaction at a level of their choice (this may be little or no social interaction)", and that they may need "support with all activities of daily living". However, evidence suggests that such sensory deprivation in combination with physical inactivity may have detrimental effects on both somatic and mental health, and strongly increase the risk of a multitude of diseases (cf. for instance Khan & Khan, 2020; and Park et al, 2020). In children and young people normal bodily, mental and social activities are pivotal for a normal development.	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS. The committee note that the level of support needed is individual to the person and

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				The guideline lacks an assessment of potential harms caused by this recommendation. References - Khan I, Khan MAB. Sensory and perceptual alterations. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Park JH, Moon JH, Kim HJ, Kong MH, Oh YH. Sedentary lifestyle: overview of updated evidence of potential health risks. Korean J Fam Med 2020; 41: 365-73.	agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.
Royal College of Paediatrics and Child Health	Guideline	007	001	The recommendation concerning the need for "a low-stimulus environment, for example a dark quiet room with interaction at a level of their choice (this may be little or no social interaction)" appears to be based primarily on data relating to adults with ME/CFS. It is unclear what the evidence base is for this recommendation in relation to children and young people; it does not appear to be addressed as a part of any of the references used in the generation of this draft guideline. Neither did it emerge as a theme in the piece of work commissioned by NICE and undertaken by the Oxford Clinical Allied Technology group; specifically, the coping strategies identified in the NICE-commissioned work were: (a) support provision from school (b) pacing and energy saving strategies (c) efficiency of referral (and also treatment in the subsequent text) (d) supportive advice and (e) practical changes. Further in the section headed "Management and coping strategies" a number of options were discussed in detail, none of which included a "low-stimulus environment, for example a dark quiet room with interaction at a level of their choice (this may be little or no social interaction)".	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.
Royal College of Paediatrics and Child Health	Guideline	008	010	The guideline recommends a slightly modified version of the SEID diagnostic criteria for ME/CFS. However, evidence suggests that the SEID diagnostic criteria lacks discriminant and prognostic validity in children/adolescents (Asprusten et al,	Thank you for your comment. The committee carefully considered the application of the criteria to children and young people in section 1.2.34 of the committee discussion in Evidence review D- Diagnosis. They acknowledge there is limited evidence but observed that the two criteria in the

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				2018). There is concern that pediatricians are recommended to use diagnostic criteria for ME/CFS of dubious quality. Reference Asprusten TT, Sulheim D, Fagermoen E, Winger A, Skovlund E, Wyller VB. Systemic exeration intolerance disease diagnostic criteria applied on an adolscent chronic fatigue syndrome cohort: evaluation of subgroup differences and prognostic utility. BMJ Paediatr Open 2018; 2: e000233.	review identified the same key symptoms as those identified in the adult criteria. The committee agreed that on this basis and reflecting on their own knowledge and experience the majority of the recommendations on suspecting and diagnosing ME/CFS could be generalised to children and young people. In addition to this the committee added additional recommendations for children and young people ensuring that they are referred to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis. This the committee hopes will ensure that children and young people will have a correct diagnosis of ME/CFS. We note the Asprunten study was in a small sample of 120 adolescents diagnosed using the NICE 2007 criteria for the diagnosis of ME/CFS.
Royal College of Paediatrics and Child Health	Guideline	010	009	1.28 - This should be extended to be a more active request of support in education, including training for school staff, awareness raising of ME/CFS for the whole school community in addition to the individual learning support plan.	Thank you for your comment. The committee agree early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and allows for further communication when the diagnosis is confirmed. The suggestions you raise are addressed in the recommendations in section 1.9 supporting people with ME/CFS in work ,education and training.
Royal College of Paediatrics and Child Health	Guideline	010	011	1.3 - Staying within the 'energy envelope' and not pushing through activity in a controlled manner would potentially impact the progression of rehabilitation. If parents and young people were difficult to engage and read the revised guidelines it would be extremely difficult to convince them that small increments in activity can be safe and beneficial.	Thank you for your comment. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they noted there is a lack of trial evidence to support that advice to rest prevents deterioration and improves prognosis

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					in people with suspected ME/CFS, but they agreed the advice not to use more energy than they perceive and to rest through would not be harmful in the short term. In addition committee noted that it is important to consider that people that are suspected of ME/CFS but not later diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone.
Royal College of Paediatrics and Child Health	Guideline	010	018	1.3.1 - The concept of an energy envelope could be misinterpreted and never being encouraged to challenge this with careful, responsive rehabilitation would leave large client groups unable to progress and make steps to improving their quality of life.	Thank you for your comment. After considering the stakeholder comments the committee agreed that the concept of an energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. The committee agreed the advice recommended would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about managing their energy and how much rest is appropriate for the individual.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

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Royal College of Paediatrics and Child Health	Guideline	010	018	1.3.1 - The term energy envelope feels restrictive and as if people could not grow in this. So much of the commentary and debate around this subject is about language, and yet the language used in this document is too complicated and sets a tone that is hard to work with.	Thank you for your comment. After considering the stakeholder comments the committee agreed that the concept of an energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. The committee agreed the advice recommended would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about managing their energy and how much rest is appropriate for the individual. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These

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					recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5).
Royal College of Paediatrics and Child Health	Guideline	011	003	1.4 - The guideline states refer to a specialist team. These are not nationwide so therefore could not always be accessed locally. There is a cost implication to this in setting up services and this could impact on existing services if they were asked to cover a larger geographical area.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. There are areas that may need support and investment to allow access to services. This guideline highlights areas where the specialist team should focus on (e.g. assessment. and development of a care plan) and those areas that should be done in primary care (e.g. initial diagnosis and review).
Royal College of Paediatrics and Child Health	Guideline	012	010	1.5.2 - This is comprehensive and good to see but should also include the carers assessment information mentioned in 1.6.12 and signposting mentioned in 1.66. The missing element is emotional health and wellbeing, of particular importance for children and young people with ME/CFS and their siblings/families as part of this management plan.	Thank you for your comment. Section 1.6 is linked to the information and support needs bullet point. After considering the range of stakeholder comments, the third bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing'.

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Royal College of Paediatrics and Child Health	Guideline	013	001	1.5.3 - If patients are expected to have a written copy of a very detailed management plan this will be time consuming to implement and if it needs regular updating this would have cost implications as will be labour intensive.	Thank you for your comment. Written materials refers to hard (paper) copies of documents. This could be printed material.
Royal College of Paediatrics and Child Health	Guideline	013	009	1.5.4 - Signposting support should accompany the management plan.	Thank you for your comment. The list includes information and support and links to the recommendations in this section including those on signposting. As with all lists and examples they are not intended to be exhaustive
Royal College of Paediatrics and Child Health	Guideline	014	009	1.6.3 - The NHS Accessible Information standard should be cross referenced here, particularly to highlight the various communication preferences/needs/adaptations that are legislated for within this statutory guidance e.g. double appointment, interpreters, communication aids, videos with results explained.	Thank you for your comment. As you state the NHS Accessible Information standard is statutory guidance It is referenced in the guideline on people's experience in adult social care services included in this recommendation. In addition it is at the start of the Recommendation section on 'Making decisions using NICE guidance'.
Royal College of Paediatrics and Child Health	Guideline	014	015	1.6.4 - This needs to include an exploration of the emotional health and wellbeing needs, building emotional resilience for the patient and their families/carers.	Thank you for your comment. This recommendation is to provide information about the impact of ME/CFS for people with ME/CFS. Emotional health and wellbeing needs are addressed in the personalised care and support plan.
Royal College of Paediatrics and Child Health	Guideline	014	015	1.6.4 - Advice to tell patients that only a small proportion of people recover or have long periods of remission goes against what is seen in practice where 95%+ of the reviewer's young people resume normal activity. Specialised teams generally follow most of the guidelines suggested: flexible appointment times, liaising with education, not discharging if missing appointments. There would be a financial impact to follow this recommendation as more specialist teams would need to be set up to respond appropriately and dedicate the time needed in managing this patient group.	Thank you for your comment and information. After considering the range of stakeholder comments the committee have edited this bullet points and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.

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Royal College of Paediatrics and Child Health	Guideline	015	027	1.6.12 - Pleased to see the reference to young carers. This could be strengthened around dual carers assessments i.e. when being medically treated, this triggers a carers assessment, or when the dual needs between children and adults' services.	Thank you for your comment and information.
Royal College of Paediatrics and Child Health	Guideline	016	012 - 015	1.7.3 - Resources are required for a 24-hour assessment by a safeguarding team with ME/CFS experience.	Thank you for your comment. After considering the stakeholder comments the reference to 24 hours has been removed to acknowledge the involvement of health and social care professionals with ME/CFS may be later in the process.
Royal College of Paediatrics and Child Health	Guideline	016	006	1.7.1 - NICE level evidence can be absent, limited or lacking but this is not evidence that it does not exist or that the alternative to considering possible degrees of inappropriate care/perspective is dismissed as only prejudice and misunderstanding. After reading the whole guideline, it was felt that the emphasis on belief reflects difficult experiences but does not acknowledge some complex examples that have arisen. It even risks compounding an illness and young person's perspective. EMDR in young people is buried in the list of mental health guideline references, the reviewer questioned whether it may be worth highlighting in the guidance, even if just to state that it is anecdotal and not evidenced. The accurately guidance states both the complexities of this condition and the fears of prejudice but it needs to be more balanced in order to make it as helpful for children as it aims to be.	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.

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					No evidence on EDMR was identified in the non-pharmacological review and the committee had little experience of its use in ME/CFS and as such have not commented on it.
Royal College of Paediatrics and Child Health	Guideline	017	008 - 019	1.7.6 - Although it says "not necessarily" it still reads as if it would be against NICE guidance to be concerned about these things, the language needs more thought.	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. The following recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability.. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
Royal College of Paediatrics and Child Health	Guideline	008 + 010	010 + 015	The guideline recommends that ME/CFS should be suspected if "the person has had all of the persistent symptoms [i.e., those required in the SEID criteria] for a minimum of […] four weeks in children and young people. Furthermore, the guidelines recommend advice on managing symptoms, such as to stay within the 'energy envelope', for persons in whom ME/CFS is suspected. It is not appropriate for every child who feels tired after four weeks to be given a provisional diagnosis of CFS/ME.	Thank you for your comment. *Suspecting and Diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the

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				In a recently conducted prospective study on fatigue development following Epstein-Barr virus infection in adolescents (12-20 years of age), patients were recruited two to six weeks after onset of the first symptoms (Pedersen et al, 2019). A novel analysis of this dataset selecting cases with ≥28 days (median 32, range 28–42) since symptom onset (n=95) showed that a total of 25 adolescents (26%) satisfied the SEID diagnostic criteria, and thus adhered to the guideline definition of "suspected ME/CFS". As the incidence of symptomatic EBV-infection (infectious mononucleosis) is at least 1% among adolescents (Cozad et al, 1996), one would expect that a minimum of 17,000 adolescents would suffer from "suspected ME/CFS" each year from this cause alone in the UK (total population 12-20 years old approximately 6.7 million). Evidence suggests a substantial spontaneous recovery rate in fatigue following infections, in particular during the first months after the preceding infectious event (Hickie et al, 2006). There is concern that the present guideline recommendation will attribute a "disease label" to a phenomenon which in the great majority will resolve by itself, resulting in unnecessary concern and anxiety, and potentially leading some individuals to adapt to a "sickness role" resulting in long-lasting disabilities. If chronic fatigue development to some extent is related to negative expectancies, as suggested by recent models (Kube et al, 2020), such "disease labelling" with the potential of reinforcing negative expectancies might lead to self-fulfilling prophecies and thus cause severe harm. It was questioned whether a risk assessment was conducted in relation to this recommendation. Furthermore, there was concern that the great increase in "suspected ME/CFS" cases that might be foreseen from the guideline recommendations might overwhelm the healthcare system. A health economy analysis of the consequences of this recommendation should be considered, taking into account the increased number of "suspected ME/CFS" cases as well as the	guideline and in more detail in the discussion of the evidence sections in the review chapters. The period of a minimum of 4 weeks is to alert clinicians to the possibility of ME/CFS. Based on the evidence and their experience the committee agreed it is important that children and young people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. They noted that the advice recommended at this stage would not be detrimental to children and young people who are then not diagnosed with ME/CFS. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed your point and added some clarity for readers. In summary the edits to the point you make are: • 'Provisional' diagnosis has been deleted for the following reasons: ○ the committee agree the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. Misdiagnosis of ME/CFS. The committee acknowledged and discussed the difficulty of removing a diagnosis of ME/CFS once it has been given. They edited the recommendations in the Diagnosis section of the guideline to ensure that the diagnosis is confirmed (or conversely, not confirmed) by a ME/CFS specialist team.

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				strong tendencies to spontaneous recovery of post-infective fatigue states. References - Pedersen M, Asprusten TT, Godang K, Leegaard TM, Osnes LT, Skovlund E, Tjade T, Øie MG, Wyller VBB. Predictors of chronic fatigue in adolescents six months after acute Epstein-Barr virus infection: A prospective cohort study. Brain Behav Immun 2019; 75: 94-100. - Cozad J. Infectious Mononucleosis. Nurs Pract 1996; 21: 14-16, 23, 27-28. - Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. BMJ 2006; 333: 575-81. Kube T, Rozenkrantz L, Rief W, Barksy A. Understanding persistent physical symptoms: conceptual integration of psychological expectation models and predictive processing accounts. Clin Psychol Rev 2020; 76: 101829.	In addition to this the committee added additional recommendations at the 4 week point for children and young people ensuring that they are referred to a paediatrician in the first instance for further assessment and investigation and then to a ME/CFS specialist for confirmation of a ME/CFS diagnosis. This the committee hopes will ensure that children and young people will have a correct diagnosis of ME/CFS. Health economics Since the committee have now removed reference to a provisional diagnosis and made recommendations about testing for alternative conditions, the demand on services should not be so great. Furthermore, the diagnostic criteria are slightly stricter than in the previous guideline. See Evidence review D- for the evidence and committee discussion.
Royal College of Paediatrics and Child Health	Guideline	020	019	Advice to provide aids and adaptations could be detrimental to the patients if given immediately as this could encourage disability rather than enabling independence. This is a very grey area that would normally be tailored to the individual after careful consideration of the potential impact. Making it more prescriptive would be risky.	Thank you for your comment. The committee agree there are risks and benefits to all strategies to support people with ME/CFS managing their symptoms and any risk, if any, will be individual to the person and should be discussed.
Royal College of Paediatrics and Child Health	Guideline	022	006	1.9.5 - As all NICE guidelines cover Wales, do they have EHCPs' in Wales?	Thank you for your comment. Currently they don't have EHCPs in Wales, there are statements of SEN and individual education plans. These are being phased out and replaced with individual development plans in September, see https://gov.wales/additional-learning-needs-special-educational-needs

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Royal College of Paediatrics and Child Health	Guideline	023	017	1.10.5 - The reviewer was pleased to see the inclusion of transition.	Thank you for your comment.
Royal College of Paediatrics and Child Health	Guideline	026	General	The section on energy management/exercise/physical maintenance is very confused with no non structured exercise, but structured exercise if it's not GET etc. as well as reduce your activity, but must do activity to reduce risk of contractures etc. It is long, and often contradictory and even to the reviewer's team has been a really confused read as to what could be offered. It suffers from both being too didactic and too loose and would benefit from some editing and a better overview of some general principles before going into detail.	Thank you for your comment. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS.

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					See evidence reviews F and G Non-pharmacological management for further information on physical activity and exercise. *Physical maintenance* After considering the stakeholder comments about the physical maintenance section this section has been edited to add some clarity for readers. In summary the edits are: • The section has been renamed to physical functioning and mobility and moved to the symptom management section • text has been added to the first recommendation to clarify this is about strategies to maintain and prevent the deterioration of physical functioning and mobility • text has been added that this should be small amounts and throughout the day to clarify this is in the context of the priorities that people may have • strength and endurance has been replaced by muscle function.
Royal College of Paediatrics and Child Health	Guideline	027	021	1.11.15 - Advising patients not to exercise if not part of a 'supervised' programme could be misinterpreted; a young person would be disempowered if they believe that they can't undertake exercise to prescribed guidelines agreed in advance without 1:1 supervision. In practice the reviewer would set a programme in agreement with the young person, but they sometimes feel confident enough, and prefer, to do this independently. If every exercise session had to have 1:1 supervision this would impact on costs as more staff would be needed to provide this level of service. Graded Exercise Therapy – the reviewer uses this in their service as a general guide as it works in practice (the reviewer has lots	Thank you for your comment. After considering the stakeholder comments this has been edited to,,' do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.' After considering the stakeholder comments, physical activity or exercise has been added to aid clarity in the recommendations in this section..

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				of data on outcomes in young people). The approach is however adapted for each individual as symptoms dictate. It would seem that the respondents to the study have not been seen by specialist teams so maybe had experienced a very prescriptive approach to GET with no adaptations for individuals. The reviewer felt that some form of graded exercise needs to remain in the guideline as it succeeds in practice, even if it is described differently to not appear as rigid. The need for specialist physiotherapy or OT is recognised but this will have a huge cost implication as it needs to be nationwide.	Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical

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					effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of

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					the recommended services across the NHS. There are areas that may need support and investment, such as training costs, to implement some recommendations in the guideline.
Royal College of Paediatrics and Child Health	Guideline	030	014	1.11.27 - Are there other guidelines relating to pain for children and young people to include?	Thank you for your comment. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. There are no other guidelines relating to pain in children and young people.
Royal College of Paediatrics and Child Health	Guideline	034	002	1.11.43 - Are there other areas of psychological support that could be explored for children and young people, such as using the https://www.annafreud.org/mental-health-professionals/thrive-framework/.	Thank you for your comment and information. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).
Royal College of Paediatrics and Child Health	Guideline	039	027	1.14.6 - Offering a review with children every 6 months only will not satisfy the home-schooling requirement of three-monthly reviews.	Thank you for your comment. The recommendation is 'at least every 6 months' allowing for more frequent reviews if necessary.
Royal College of Paediatrics and Child Health	Guideline	040	001	1.14.7 - As before, inclusion of the impact on emotional health and wellbeing should be explored for children and young people.	Thank you for your comment. The recommendation on what to include as a minimum as part of the review includes psychological, emotional and social wellbeing. In NICE guidelines people/person (with ME/CFS) refers to adults, young people and children.
Royal College of Paediatrics and Child Health	Guideline	040	011	1.15 - The reviewer agrees that regular training is required but this would have funding implications. Funds would need to be made available to cover costs.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as training costs and access to ME/CFS specialist services, to implement some recommendations in the

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					guideline. However, this guideline highlights areas where resources should be focussed. A strong theme from the evidence was the lack of understanding about ME/CFS and training in health and social care professionals and the committee agreed it was important to make recommendations about training. Your comments will also be considered by NICE where relevant support activity is being planned.
Royal College of Paediatrics and Child Health	Guideline	042	010	The definition of exercise ('Exercise is planned, structured, repetitive and purposeful activity focused on improvement or maintenance of one or more components of physical fitness. Exercise is a subcategory of physical activity') may apply to adults but is not a definition that is used in childhood, or in paediatric services. Children exercise all the time, particularly at school during their breaks. The main criticism of treatment programmes for ME/CFS (evidence submitted to NICE) is in making children reduce exercise, particularly exercise which is spontaneous and unplanned. NICE can choose to define a treatment programme in this way but cannot define exercise in this way for children as it will provide confusion for those providing services as well as parents and carers.	Thank you for your comment. The Definitions for the terms 'Exercise' and 'physical activity' are based on those used by the World Health Organisation and are widely understood. We are not aware of any source that uses the term 'exercise' to describe break time play at school, which is more correctly described as either 'active play' or 'active recreation'.'
Royal College of Paediatrics and Child Health	Guideline	056	008	The reviewer agrees with the descriptive information in the recognition statements but does not feel that in its present wording this guideline will improve the consistency of best practice without more attention to details around affected children. It may require increased resources for Trusts to create the quality of specialist teams and independent information gathering and perspective required.	Thank you for your comment. The committee did not feel able to give more detailed recommendations on safeguarding. It is acknowledged elsewhere in the guideline that development of specialist teams will require investment in some areas.
Royal College of Paediatrics and Child Health	Guideline	060	019	The sections on impact on resources have recommended earlier referral and specialist input. This is justified as it means outcomes will be better. However, there is no evidence to support this, and given the fact that the guidance also says there is no treatment or cure for ME/CFS, and is highly negative about outcomes, it seems contradictory to then make recommendations that will end up "saving money " and being cost-effective in the end as no evidence has been presented to back this up.	Thank you for this comment. This recommendation is to make people aware that no intervention has been shown to cure ME/CFS. The committee did not make this recommendation to save money but instead to inform patients and clinicians. Even in the trials, which showed statistically significant improvements in outcome, still show poor mean outcomes after treatment.

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Royal College of Physicians and Surgeons of Glasgow	Guideline	General	General	The Royal College of Physicians and Surgeons of Glasgow although based in Glasgow has a membership of 15,000 and represents Fellows and Members throughout the United Kingdom. While NICE has a remit for England, many of the recommendations are applicable to all devolved nations including Scotland. They should be considered by the relevant Ministers of the devolved governments. The College recognises that ME/CFS is difficult to assess and treat. ME/CFS is a symptom complex and not a well-defined disease, with a spectrum of manifestations. The pathophysiology as the reports states is unclear. The report suggests it is a distinct entity whereas there is a clear overlap between ME/CFS, Chronic Pain Syndromes, Fibromyalgia, Psychiatric disease with physical symptoms (eg Depression) and the emerging Long COVID spectrum. The reviewing Committee's expertise has a clear bias to the paediatric spectrum and much of the report appears only relevant to children and young people yet covers adult years. The Committee does not appear to have members who have a background in rehabilitation, neurology, musculo-skeletal medicine, psychiatry (although there is a psychologist) or the chronic pain aspect of anaesthesia. Usually, NICE guidance relies on clear evidence of benefit from literature. Where there is no evidence or it is confused, no or few recommendations are made. While it is acknowledged that this is a difficult area, the recommendations appear aspirational rather than based on evidence. Even where the text says that evidence is mixed (for example Cognitive Behavioural Therapy), there is still strong recommendations that it should be provided and people with ME/CFS should have access to this treatment.	Thank you for your comment. *Diagnosing ME/CFS* Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms, particularly with the addition of PEM . Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015). The committee note that this differentiates ME/CFS from other conditions where pain is the dominant symptom. The discussion section of Evidence review D- Diagnosis includes a list conditions that commonly occur in people with ME/CFS and has the examples you have listed *Committee composition* The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. As you note a clinical psychologist with experience in delivering CBT to people with ME/CFS was recruited to the committee. *Decision making*

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				It is often difficult to ascertain which recommendations are evidence based and which are not. NICE has developed its guidance to be evidenced based and then to use health services resources effectively. The recommendations made do not appear to be evidenced based. Many of the services are not available in many areas of the UK. There does not appear to be an economic assessment of the benefits or otherwise of the recommendations. There is wide literature in this area with little which is conclusive. The surrogate when the evidence base is poor will be custom and practice by acknowledged experts in the field. However, this report has not used all the specialities involved in management of ME/CFS and its recommendations go beyond what is expected from custom and practice. These difficulties should be discussed and acknowledged in the report.	One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence , in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences.. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). It is difficult to quantify the cost and benefits of the committee's recommendations and therefore a formal economic evaluation has not been possible. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, to implement some recommendations in the guideline. This guideline highlights areas where resources should

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					be focussed and those interventions that should not be recommended, saving resources in other areas.
Royal College of Physicians and Surgeons of Glasgow	Guideline	008 + 042	017 014	The term fatigable has a specific neurological definition, namely decline in performance during continuous performance of a prolonged task. While this may be present in ME/CFS and other neurological disorders, the definitions given for fatigability include other examples of neurological fatigue.	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change fatigability. This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS,' Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.', **'**The committee hope this has added some clarity for readers.
Royal College of Physicians and Surgeons of Glasgow	Guideline	028	006	This implies that all graded exercise therapies are based on fixed incremental increases in physical activity or exercise. In fact, most of the studies using graded exercise therapies used incremental increases which were not fixed. A more accurate description would be 'do not offer any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy *with fixed incremental increases'.*	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This

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					has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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Royal College of Physicians and Surgeons of Glasgow	Guideline	037	001 and many others	The term flare is used widely in the text. Flare implies an inflammatory process which is not the case in ME/CFS. The pathophysiology of this condition is uncertain and therefore the term exacerbation is more appropriate.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly CFS/ME Service	Guideline	General	General	As CFS/ME is often known to have an infective trigger, the exclusion of any reference to Covid infection, post covid fatigue, or long covid represents a lost opportunity to support these patients and services and galvanise resources to the patchwork of CFS/ME services. A separate guideline on Covid and or Long Covid only promotes to divide understanding of the mechanisms of how CFS/ME occurs and keeps CFS/ME as a marginalised conditions. EBV is the most frequent trigger for the condition in children and not to mention an infective trigger from our experience of offering services for this patient group will continue to encourage others to see it as all psychological and not needing medical oversight.	Thank you for your comment. At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations. NICE are developing and updating the COVID-19 rapid guidelines in order to reflect that evidence.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly CFS/ME Service	Guideline	006	008	1.1.8 - Fatigue and Post exertional fatigue or malaise or PESE needs to be described at the top of this section.	Thank you for your comment. The committee agree that this section is important. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.

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					The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience including fatigue and post exertional malaise.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly CFS/ME Service	Guideline	008	005	1.2.2 - Functional assessment and cognitive and sensory assessment should be included. Mental health assessment which includes a suicide screen as well as/ or a psychological assessment might be a more flexible term . Many services have Occupational Therapist who can provide this more rapidly and in the community.	Thank you for your comment. The clinical history bullet point now includes the examples 'relevant symptoms and history, comorbidities, overall physical and mental health' to cover these assessments.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly CFS/ME Service	Guideline	010	022	1.3.2 - Returning for a medical review has massive implications for services that traditionally have no or only a few hours of medical time. We are inheriting a legacy of poorly resourced services, how can the guideline inform commissioners of the need to fully resource services if this is a recommendation and subsequently patient have a raised expectation to have access to this.	Thank you for your comment. This recommendation is good practice, anyone with new symptoms or worsening symptoms with or without a diagnosis should contact a healthcare professional for a review. In addition the committee based the recommendation on the qualitative evidence (see Evidence reviews A and C) that people with ME/CFS in the early stages of their condition felt ignored and disbelieved.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly CFS/ME Service	Guideline	018	020	1.8.4 - Hospital care should also include attendance at an outpatient clinic not just a bed stay.	Thank you for your comment. The committee agree there should be flexibility in supporting people with ME/CFS accessing any hospital services and the principles in this section apply.
Royal Cornwall Hospitals NHS Trust - Cornwall and Isles of Scilly	Guideline	019 023 024	1.8.6 1.11.1 1.11.2	Should include under stimuli "using a lowered tone of voice and using calm movements and gestures." Should say no medical treatment. Many patients do well with rehabilitation ie learning symptom management and strategies and adapting their life styles. There needs to be a positive	019 These are examples of what to consider in facilitating a low stimulus environment in a hospital, it is not meant to be exhaustive and for this reasons your suggestions have not been added.

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CFS/ME Service		025 026 026 027 029 034 039 050	1.11.6 1.11.8 1.11.11 1.11.5 1.11.21 1.11.43 1.14.1	reflection of those that do "recover" not just a a blanket statement like this. Many service use Activity Management as supported in the NICE Guideline 2007 this has been the most successful approach with patients and literature, resources and books refer to it as such. To avoid confusion with patient, or reinventing the wheel can it be called Activity and Energy Management. Reducing this is not always appropriate when anxiety is or has become a predominant issue. This section seems out of context most specialist services have OT and Physiotherapist and the guideline has already mentioned referral to specialist service for symptoms management and reduced activity level before and after this section. Extending activity either physical, cognitive or emotional is part of tailoring and activity and energy plan so this is seems to be saying the same thing twice, unless you are talking about aerobic activity or exercise as per a GET approach and not wishing to mention the name. Should say hypermobility also This is problematic. Many patients want to address deconditioning, and want to include physical activity as part of a treatment programme such as walking swimming or cycling. Incremental increases are the way to do this so that any increases in symptoms can be management or stopped or scaled back. I think what you might be suggesting is that any treatments that suggest this should be part of an agreed plan with patients with their full consent. Which you almost say in 1.11.17 so why include 1.11.5 and 1.11.16 are confusing this with exercise? Occupational Therapists is missing from line 8, as Occupational Therapists use activity as a treatment medium this includes physical activity.	*Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. 1.11.2-1.11.10 This section is called energy management. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity (see Evidence review G for the committee discussion on self-management strategies). After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase or worsening of their symptoms. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option (recommendation 1.11.8) Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See

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				This should say " CBT and goal orientated approaches" you switch to using the term health care professionals so this could then be delivered by those without specialist knowledge of CFS/ME. I am not sure that is useful. Routine or full bloods should be taken at least once a year in primary care if the person is no longer in specialist services to rule out slowly developing diseases eg thyroid etc There is already an agreed National Outcomes Data Set for adults and Childrens CFS/ME see past 2007guideline.	evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Deconditioning* 1.11.11 After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. *1.11.21* *This recommendation does not include an occupational therapist because if a physical activity or exercise programme is offered, the committee agreed it should be overseen by a physiotherapist in a ME/CFS specialist team.* *CBT* This section refers specifically to CBT and not any other approaches. It is clear in the recommendation that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for

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					ME/CFS. This does not suggest that CBT could be delivered by healthcare professionals without specialist knowledge of ME/CFS. *Blood tests* Throughout the guideline the committee have recommended the importance of carrying out investigations to identify other conditions or exclude other diagnoses. The committee have now included examples of investigations that might be carried out in the suspecting ME/CFS section. *Outcomes* This refers to the development of core outcomes sets for research, to date one for ME/CFS has not been developed. See https://www.comet-initiative.org/
Science for ME (S4ME)	Guideline	General	General	Introduction to our submission Our submission is based on extensive discussions of the guideline by members of a science-focused ME/CFS online forum (Science for ME), which has a diverse membership that includes people with ME/CFS of all severity levels, carers, scientists and clinicians. We thank the ME/CFS guideline committee and NICE staff for their good work on this guideline to date. The outcome, as evidenced by the draft, is a significant step towards improving services for people with ME/CFS and correcting stigmatising views and approaches. We commend the committee for the thoroughness and scientifically sound approach of their examination of the research into therapies intended to treat or cure ME/CFS.	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that

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				We ask the committee to be equally rigorous in their use of evidence for other aspects of their recommendations. Having given careful consideration to the guideline recommendations and supplementary documentation, we provide detailed recommended changes which would better reflect the outcomes of the evidence reviews, while removing some of the assumptions and decisions based solely on the committee members' experience. We highlight here three main areas of concern: 1. Diagnosis: We agree that the IOM (Institute of Medicine) criteria form a suitable basis for clinical diagnosis. However, the committee has made significant changes to the IOM criteria which will exclude a number of people from being diagnosed with ME/CFS, despite meeting the requirements of the IOM criteria. We do not think the experience of a small committee is an adequate basis for creating new untested criteria with the result that people who do not exhibit cognitive difficulties may be denied appropriate diagnosis and condition management, potentially leading to harm. 2 Management: People with ME/CFS need input from medical and care services to help them learn how they can manage their limited energy in order to reduce the occurrence of post-exertional malaise (PEM) and long term deterioration. We have recommended a more straightforward self management approach using symptom-contingent pacing, with guidance as needed from specialist nurses who can also help with managing symptoms, including reviewing medications, with making necessary life changes, and by providing informal wellbeing support for those who want to talk about feelings that arise naturally as a result of living with a chronic debilitating illness. Physical activity	were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *1.Diagnosis* See Evidence review D – diagnosis for the evidence on diagnostic criteria and the committee discussion section explaining why the committee recommended that all four criteria should be present. This includes your point about including cognitive difficulties. In summary the committee maintain that cognitive difficulties are a key symptom in suspecting ME/CFS and are commonly reported in people with ME/CFS. They note that cognitive difficulties (such as brain fog) are described in most of the criteria (7 of the 9) criteria) reviewed in Evidence review D in contrast with orthostatic intolerance (4 of the 9 criteria) supporting further their experience and expertise and this has been clarified in the discussion section of the report. *2.Management* After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily

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				programmes for those whose symptoms have improved, and CBT for psychological support, are neither evidence based, nor necessary. We recommend they be removed from the guideline, where their inclusion presents a real risk of harm, with GET and directive CBT continuing to be provided under different names. 3 Terms used in the guideline: We are concerned that some of the terms introduced or defined are an unnecessary departure from current usage by clinicians, researchers, people with ME/CFS and in publications. This will add a further layer of misunderstanding and hamper communication between people with ME/CFS and their clinicians. Of particular concern are the introduction of the colloquial and easily misinterpreted 'energy envelope' and 'flare'; the complete lack of mention of 'pacing'; and the renaming of the almost universally recognised term 'post-exertional malaise', which has been replaced with the vague and misleading 'post-exertional symptom exacerbation'. The recommendations that address the requirements of people with severe and very severe ME/CFS will make a real difference to wellbeing for many with ME/CFS. We have noted that people with less severe illness may also require similar accommodations, especially during periods of deterioration. Finally, we note that the improvements to the guideline are a necessary, important step, but it will take commitment and cooperation from many to achieve the complete re-orientation of ME/CFS services that is required. We urge the committee to build into the guideline safeguards and requirements for accountability to ensure that the promise of evidence-based patient care is realised.	living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS. GET *Provision of care*

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					The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Terms used in the guideline* The committee agree that there are many different terms used across the ME/CFS research, clinical and patient communities and the committee have taken care to define the ones used in the guideline. The committee discussed the use of the term

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					pacing agreed that it means something different to different people with many versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms: • Energy envelope to energy limits. The committee noted the concept of describing the amount of energy a person has to do all activities without triggering an increase in their symptoms remains the same. • Debilitating fatigability. This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS • Flare to flare up *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.

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Science for ME (S4ME)	Guideline	General	General	Medical care models and the use of evidence. NICE guidance for the management of conditions for which there is no effective treatment must be based on the best available evidence, just as it is for conditions for which there are effective treatments. Where the guideline cannot make evidence-based recommendations that may lead to improvements, it must fulfil its brief to ensure recommendations do not lead to deterioration or harms. We ask the committee, in reviewing stakeholder feedback and amending the guideline, to examine the approach they have used in developing their recommended model of care, the assumptions underlying the recommendations, and whether the included recommendations are well supported by their own evidence reviews. The committee has made recommendations that can be implemented by minor adaptations to current service provision utilising the therapist specialisms that are currently providing CBT and GET as treatments for ME/CFS. This may have the short-term advantage of causing minimal upheaval to services, upset to healthcare professionals with entrenched beliefs about cause of or appropriate treatment for ME/CFS, and prima facie appear to be cost-efficient. It may also seem that switching from providing programmes on GET or CBT to courses on 'energy management' is a good fit, with CBT therapists providing psychological support as they do so. However, the clinical effectiveness evidence for CBT for ME/CFS was all of low or very low quality (Evidence Review G, pp.72-119, p. 318 line 23). There can therefore be no justification for provision of ME/CFS services by CBT therapists, as to provide support for other aspects of care, such as energy management or medical symptoms, would exceed the bounds	Thank you for your comment and information. CBT/GET The trial evidence showed that CBT is cost effective for people with ME/CFS, even though the health gain was quite modest. *Provision of care* The evidence showed that people with ME/CFS value access and support from health and social care professionals that understand ME/CFS (evidence reviews A,B,C and I). The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee have recommended that certain interventions should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive

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				of their expertise and risk harm to people with ME/CFS. Services staffed by healthcare professionals (HCP) who have provided GET and CBT as treatment for ME/CFS for years are likely to continue to foster a shared mindset amongst staff that ME/CFS can be treated by increasing physical activity or changing thoughts and behaviours. Retraining of such staff is unlikely to be adequate to prevent old methods from creeping into updated approaches, and harms to people with ME/CFS from resulting. It should also be self-evident that provision of CBT for ME/CFS is not cost-effective because there is no good quality effectiveness evidence to support it. In the review of qualitative evidence, themes of validation, relationship with therapist and support were found not to be specific to CBT (Evidence Review G, p.324 lines 41-43). Support, validating patient experience, listening and building rapport are elements of care that may be provided in interactions with any healthcare professional (HCP). Our members report that the natural reactions to living with a chronic debilitating disease, such as frustration and sadness, are often helped more by assistance with the practicalities of the major upheaval to their lives, and from ready access to an HCP who understands all aspects of their condition, than from undergoing a psychological therapy, which itself depletes already scarce energy and may lead to worsening. There is likewise no reliable evidence to support the recommendations for physical activity programmes for some people with ME/CFS, or to suggest that increasing by flexible increments while remaining within a person's 'energy envelope' is feasible as a concept, has benefits (as suggested at 1.11.19) or is safe. The recommendations in the subsection on 'Physical activity' present a form of graded exercise therapy, for which the evidence review established, there is no reliable evidence. The portrayal in the guideline of activity programmes involving fixed	clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Symptom management* The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS. *Training* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering

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				increments as being poorly evidence and potentially harmful, and programmes involving flexible increments as acceptable and potentially beneficial is a false distinction, since it is clear that clinical studies of GET included in the effectiveness review did include non-fixed increments. There is no reliable evidence that people with ME/CFS who find their energy levels have improved would benefit from input from HCPs, with the possible exception of those transitioning from being bedbound to greater levels of mobility, for whom the recommendations under physical maintenance may be helpful alongside general advice and supervision from a physiotherapist with up-to-date ME/CFS training consistent with this guideline. Our members generally report being able to increase activity levels naturally without need of HCP input when they have experienced improvements in health. Such a 'hands-off' approach has the benefit of entailing no cost to the health system. The third area of management covered by the draft guideline is symptom management. In contrast to the level of detail and specification of models for energy management and the new versions of CBT recommended, there is very little in the way of detail on symptom management. Yet, for many people with ME/CFS, the main reasons for seeking assistance from health and care services relate to new or worsening medical symptoms of ME/CFS, which may be severe or very severe, including orthostatic intolerance, pain and gastrointestinal symptoms, and seeking help with the practicalities of making major life changes and arranging care needs. To adequately assist with such issues without exceeding competence or bounds of expertise, the HCP must hold appropriate qualifications in a suitable discipline and have relevant experience, and up-to-date training consistent with this guideline. Currently, there is no guidance as to what types of	care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *Service design- consultant led model of care* This guideline focused on clinical recommendations and the committee did not comment on the configuration and delivery of services, which can be determined locally. However the committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.

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				HCP will fulfil such roles. We therefore conclude that the model of care set out in the guideline, which will inevitably entail updating existing providers and continuing with provision of therapist-based services is neither evidence based, nor fit for purpose, and carries significant risk of continuing to cause harms of the type the guideline purports to set out to avoid. Instead we recommend a consultant-led model of care, with comprehensive support and care provided by specialist nurses. This would more closely mirror the fields and levels of expertise set out in the multiple sclerosis NICE Guideline (CG186), in which a consultant neurologist and specialist Multiple Sclerosis (MS) nurses are specified as relevant professionals to involve in the person with MS's care. Such a model would involve a specialist team led by a consultant from a relevant biomedical discipline with specialist knowledge of ME/CFS who would see new patients for thorough investigation and confirmation of diagnosis, with a team of specialist nurses providing the role of the HCP who will be the main contact for people with ME/CFS, and able to assist them with energy management, symptom management and informal psychological support. Provision of therapies such as physiotherapy, occupational therapy, and psychological support such as counselling, would be supplementary for those who want and need them. The advantages of this model: a) The nurse's skills and training enable them to help with advising and monitoring many aspects of the person's health needs, to deal with more than one issue during an interaction with the person with ME/CFS, and to liaise as needed with the consultant. This more comprehensive service is cost-effective, and is energy-efficient for the patient;	

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				b) Avoids harm, including by not facilitating the continuation of the unevidenced treatments of physical activity programmes and CBT, or the stigmatising ideas that underpin them; c) General practitioners are supported with access to specialist medical advice, while time-consuming patient education and support functions are carried out by nurses with specialist expertise; d) People with severe or very severe ME/CFS and their families and carers would receive specialist support. This provision of a medical care model, where the nurse helps patients of all severity levels, is vital for people with ME/CFS, as any individual's severity level can worsen rapidly, with the need for provision to be already in place for accessible specialist ME/CFS care. Finally, we set out the aims for medical care and support provision that we consider should guide the inclusion of any recommendation in this guideline: 1. Evidence based: That all treatment offered, whether intended to be curative, to improve symptoms or to prevent worsening, be based on high quality scientific evidence. 2. First do no harm: That all medical and therapeutic care provided does no harm, whether by allowing harmful treatments to continue under new names, or by lack of provision of appropriate services that meet the needs of people with ME/CFS. 3. Accessible: That for people with ME/CFS of all severity levels, the provision of care can be accessed when needed in a	

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				form the patient can cope with without detriment to their health, and that takes account of their specific needs and limitations 4. Expert: That the person providing the advice, treatment or care has appropriate qualifications and experience, as well as up-to-date knowledge of ME/CFS in accordance with this guideline. 5. Efficient - in terms of cost, time and energy of the patient: With the same person understanding and able to advise on all their health needs, not having to see different people for energy and symptom advice and support with coping with life changes etc. 6. Consistent: medical support and care is provided by a single HCP who knows the person with ME/CFS and their needs, and can either help or refer on if needed.	
Science for ME (S4ME)	Guideline	General	General	We have made comprehensive and detailed suggestions for changes to the draft guideline and we are only one of many stakeholders making a submission. The total amount of feedback for the Guideline Committee to consider will be large, with some points likely to provoke strongly opposing views. We therefore encourage the Committee to ensure that they have sufficient time to consider the stakeholder feedback and if necessary take longer than planned in doing so. We are sure that people with ME/CFS will understand some delay in order to produce the best possible guideline.	Thank you for your comment.
Science for ME (S4ME)	Guideline	General	General	Medically Unexplained Symptoms (MUS) When ME/CFS is mischaracterised as 'medically unexplained symptoms' (MUS), 'ME/CFS' may be viewed as a term for a cluster of non-specific symptoms overlapping with other poorly understood conditions (e.g. IBS) and undiagnosed symptoms, rather than as a term for the distinct medical condition, ME/CFS, as NICE acknowledges it to be.	Thank you for your comment. Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care

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				Approaches used for MUS (also referred to as 'persistent physical symptoms' (PPS)) are likely to be completely inappropriate for people with ME/CFS and may include physical activity programmes and CBT as treatment for MUS. This guideline recognises that these approaches should not be offered as treatments for ME/CFS and are potentially harmful. Services and clinicians taking this approach are unlikely to take the limitations imposed by post-exertional malaise and the absence of reliable effectiveness evidence for the application of MUS treatment approaches to ME/CFS adequately into consideration. Any characterising of ME/CFS as MUS therefore creates significant risk of harm to people with ME/CFS, both to their health and by causing a loss of trust in the health system, with no mitigating benefit. Therefore, in order to protect people with ME/CFS from harm, we ask that the guideline makes it clear that people with ME/CFS should not be referred to MUS services, and ME/CFS should not be framed as MUS (or PPS or similar terms) for diagnosis, assessment, management, treatment or any other purpose.	and support plan, advice on energy management, physical activity, and dietary strategies.
Science for ME (S4ME)	Guideline	004	016 - 018	This clause should also recognise that ill-informed attitudes to ME/CFS have led to real harm for many people with ME/CFS. Suggested wording: '*Recognise that people with ME/CFS may have experienced prejudice, disbelief, felt stigmatised and been harmed by people who do not understand their illness*.' Thank you for acknowledging the prejudice that people with ME/CFS experience and pointing out its impact on perceptions of and willingness to engage with health services.	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience. The current wording addresses this and your suggestion does not add further clarification. For this reason the recommendation has not been edited.
Science for ME (S4ME)	Guideline	004	005 - 006	The first bullet point of 1.1.1 should include that onset of ME/CFS is typically triggered by an infectious illness.	Thank you for your comment. This bullet point has been edited to,' and its pathophysiology remains under investigation' to clarify that there is not enough

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					evidence to make any conclusions about the pathophysiology of ME/CFS and this is an active area of research. The context also includes that it is not clear what causes ME/CFS and notes that in many cases, symptoms are thought to have been triggered by an infection.
Science for ME (S4ME)	Guideline	004	010 - 011	The term 'substantial incapacity' is vague and the clause does not adequately convey the impact of severe and very severe ME/CFS or acknowledge the impact of ME/CFS for mild cases. Suggested wording: '*varies widely in severity - from mild ME/CFS where there is significant debility and greatly reduced capacity for activity to severe and very severe ME/CFS, where the person is bed-bound and requires comprehensive personal care*.'	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. The severity of the impact of ME/CFS has been recognised throughout the development of this guideline. The scope included people with severe and very severe ME/FCS as a population for special consideration and each review highlighted any relevant evidence. In addition recognising the lack of evidence NICE commissioned a report to ensure the views of people with severe and very severe ME/CFS were include in the guideline (Appendix 2_People with severe ME/CFS) and this was considered alongside the other evidence by the committee. When making the recommendations the committee considered people with severe and very severe ME/CFS separately and made additional recommendations where relevant. After considering the stakeholder comments the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe

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					ME/CFS were not hidden within the guideline and had more emphasis.
Science for ME (S4ME)	Guideline	004	14-15	The words, '*ranging from being able to carry out most daily activities to severe debilitation*' should be deleted. It incorrectly gives the impression a given person with ME/CFS may range between being able to carry out most daily activities to severe debilitation over 'days, weeks or longer', implying severe and very severe ME/CFS may remit significantly over short time frames.	Thank you for your comment. This has been deleted.
Science for ME (S4ME)	Guideline	004	005	The word 'complex' should be deleted. The underlying pathology is unknown so cannot validly be described as 'complex'. 'Complex' can be misunderstood to imply inaccurately that there are complex 'biopsychosocial' factors. It can also subtly imply that patients are 'difficult'.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change condition for disease and keep complex, to indicate ME/CFS is multifaceted and complicated. This does not imply that patients are difficult.
Science for ME (S4ME)	Guideline	004	007	The words 'can have' should be replaced with 'has'. i.e., '*[ME/CFS] has a significant impact on people's (and their families and carers') quality of life*'. ME/CFS has a significant impact on the lives of all people with ME/CFS, regardless of severity level.	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS.
Science for ME (S4ME)	Guideline	004	010	The words '*affects each person differently*' should be deleted. This is true for all medical conditions. Highlighting it here suggests more variability than is the case and may lead to misdiagnoses. Diagnosis requires meeting specific criteria (section 1.2).	Thank you for your comment. The committee disagree one of the defining features of ME/CFS is variation in the impact symptoms can have. This can be within the criteria identified for suspecting and diagnosing ME/CFS.

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Science for ME (S4ME)	Guideline	004	013	The words 'change unpredictably' should be qualified with 'sometimes', i.e. 'symptoms can sometimes change unpredictably'. There is often considerable predictability of nature and severity of the symptoms of ME/CFS. This predictability is the foundation of symptom-contingent pacing with the aim of avoiding post-exertional malaise (PEM).	Thank you for your comment. This bullet point highlights that symptoms 'can change unpredictably this doesn't infer it is always unpredictable. The addition of 'sometimes' does not add further clarity and not been added.
Science for ME (S4ME)	Guideline	004	015	We suggest addition of a fifth bullet point to 1.1.1, stating that there is no evidence that ME/CFS is a psychosomatic condition or caused or perpetuated by emotional distress or personality traits	Thank you for your comment. The committee agree that it is important to have raise awareness and have clear statements about the reality of ME/CFS. The recommendations in the principles for care section do this, the first recommendation states the reality and seriousness of ME/CFS as a medical condition. The second recommendation acknowledges that people with ME/CFS have experienced disbelief and stigma. The addition of a fifth bullet point does not add further clarity and not been added.
Science for ME (S4ME)	Guideline	005	009 - 014	We are pleased to see recognition that people with ME/CFS need early and accurate diagnosis, and regular monitoring and review.	Thank you for your comment.
Science for ME (S4ME)	Guideline	005	015 - 018	Include that refusal of assessment for and development of the 'management plan' or refusal to restart any part of it should be acceptable without this affecting other aspects of care. Suggested wording: '*Explain to people with ME/CFS and their family or carers (if appropriate) that they have the right to decline assessment for and development of the* management plan (medical care plan), *or to decline, withdraw from or refuse to restart any part of their management plan and it will not affect other aspects of their care*.'	Thank you for your comment. The committee agreed your suggestion was included in the recommendations and for this reason have not made any edits. In addition the box at the beginning of the guideline states that people have the right to be involved in discussions and make informed decisions about their care, as described in making decisions about your care.
Science for ME (S4ME)	Guideline	005	003 - 004	What is meant by, '*acknowledge to the person the reality of living with ME/CFS and how symptoms could affect them*'? The meaning of this clause is not clear. We suggest that for clarity, this bullet point be broken down into two bullet points: Suggested edit: 1. '*Provide the person with ME/CFS with information about the*	Thank you for your comment. This recommendation is supported by the evidence and supported by the committee's experience. Lack of belief in ME/CFS and understanding about the impact of their symptoms was reported by people with ME/CFS in Evidence review A, Appendices 1 and 2. This recommendation supports good clinical

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				condition, including information on how it is likely to affect their daily life. See section 1.6 Information and support.' 2. '*Listen to and acknowledge the person with ME/CFS' account of their experience of living with ME/CFS and its symptoms and how these affect them. Do not seek to minimise the impact of the illness*.'	practice in building relationships between healthcare professionals and people with ME/CFS. As you note your first suggestion is addressed in section 1.6 and for this reason not added. Do not seek to minimise the impact of the symptoms is inherent within acknowledging the reality of ME/CFS and the impact of symptoms and does not add further clarity and for this reason has not been added.
Science for ME (S4ME)	Guideline	005	005	We are pleased to see inclusion of recommendations on building supportive, trusting and empathetic relationships.	Thank you for your comment.
Science for ME (S4ME)	Guideline	005	008	We suggest inclusion of a fifth bullet point in 1.1.3, as follows: *'ensure that the person with ME/CFS is fully informed about and involved in all aspects of the planning and delivery of their care.'*	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Science for ME (S4ME)	Guideline	005	016	We consider the term 'medical care plan' to be more appropriate than 'management plan'. The former makes it clear that it is a plan to deliver care. The term 'management plan' implies that the person with ME/CFS and their condition are to be managed. All uses of 'management plan' throughout the draft guideline should be changed to 'medical care plan'.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Science for ME (S4ME)	Guideline	005	018	There are no treatments for ME/CFS, so what treatments or otherwise are being referred to in using the term 'intervention'? The term 'intervention' should not be used. It has connotations of people being told 'hard truths' about their behaviour in order to bring about improvement. As there is no treatment for ME/CFS,	Thank you for your comment. The management and management of symptoms sections of the guideline set out the strategies and treatments to support people with ME/CFS with managing their symptoms. Intervention has been replaced with treatment to match the rationale and impact section for these recommendations.

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				the types of medical assistance that can be provided may be better termed 'support' than 'intervention'.	
Science for ME (S4ME)	Guideline	006	007 - 029	We suggest renaming the subheading 'Awareness of severe or very severe ME/CFS and its impact' to 'Symptoms of ME/CFS and their impact'. Replace 'Be aware that people with severe or very severe ME/CFS' (line 8) with 'Be aware that people with ME/CFS'. While people with severe and very severe ME/CFS may experience these symptoms all of the time, people with less severe illness may also experience these symptoms, particularly during PEM. Remove 'and constant' from the clause 'severe and constant pain' (line 12) Remove the words 'severe or very severe' from line 28 (1.1.9). Add a subheading, 'People with severe or very severe ME/CFS' at page 7 line 17 before 1.1.10. 1.1.8 and 1.1.9 would then address all people with ME/CFS of all severity levels, and take into account that while people with severe or very severe ME/CFS may experience symptoms in 1.1.8 and require recognition of the impact of symptoms as detailed in 1.1.9 all the time, symptoms and debility for people with mild or moderate ME/CFS may match those of severe or very severe ME/CFS during PEM or prolonged deterioration. The guideline should not give the impression (as it does currently) that mild and moderate ME/CFS does not involve these symptoms impacting wellbeing, communication, mobility and ability to interact with others and care for themselves. Accommodations need to be made to help people with ME/CFS of all severity levels avoid over-exerting and triggering PEM or prolonged deterioration (relapse).	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. The following section on suspecting ME/CFS includes the symptoms that all people with ME/CFS experience and those symptoms that are commonly associated with ME/CFS and now precedes this section. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.

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Science for ME (S4ME)	Guideline	006	007 - 027	We think this section represents a significant advance in clearly stating the needs of people with severe and very severe ME/CFS and how these can be met. We include a reaction of an S4ME forum member with ME/CFS to illustrate this: '*it made me cry with happiness when I read it - and the sense of sheer relief in this house when we read it. I just ask that it does not get diluted down, please, because this section will help me not only with hospital care, but social services, with my MP, with housing, even just other people personally...with every aspect of my life.*'	Thank you for your comment. The committee agree that the needs of people with severe ME/CFS are very important and after considering stakeholder comments the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline.
Science for ME (S4ME)	Guideline	006	014 - 015	It should be made clear that exposure to light, sound, touch, movement and extremes of temperature if poorly tolerated can lead to PEM. For those with severe sound sensitivity, exposure to sound can cause rapid and potentially long-term deterioration.	Thank you for your comment. This recommendation describes the symptoms people with severe and very severe ME/CFS may experience and for this reason your suggestion has not been added. PEM and energy management is described in more detail in the suspecting ME/CFS and management sections of the guideline.
Science for ME (S4ME)	Guideline	006	020 - 021	'insomnia' should be added to the bullet point on sleep disturbance.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	006	022 - 023	'gastroparesis' should be added to the bullet point on gastrointestinal difficulties.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	006	026 - 027	This should be amended to reflect that there are other subtypes of orthostatic intolerance not listed here. Suggested phrasing: 'orthostatic intolerance. People with severe ME/CFS may only be able to be upright for a very short time, if at all, before experiencing symptoms including dizziness, pallor, nausea and vision problems.'	Thank you for your comment. Orthostatic intolerance and autonomic dysfunction have been added to clarify postural orthostatic tachycardia syndrome (POTS) and postural hypotension are examples of orthostatic intolerance.

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Science for ME (S4ME)	Guideline	006	014	The term 'noise' should be replaced with the term 'sound' here and for every use of 'noise' in the guideline. 'Noise' suggests that sound must be loud to a person of normal hearing to be problematic to a person with ME/CFS. This is not the case; quiet sound can be extremely difficult to tolerate for people with ME/CFS with severe sensitivity to sound.	Thank you for your comment. This has been edited.
Science for ME (S4ME)	Guideline	007	017 - 021	The guideline should acknowledge that personal care for someone with very severe ME may take more time than standard rates allow for in social care planning and that planned care may not be able to be done on days when the patient is too unwell.	Thank you for your comment. The committee agree that flexibility in accessing and providing services is important for people with ME/CFS. This is addressed further in the Access to care section of the guideline.
Science for ME (S4ME)	Guideline	007	024 - 026	The guideline should provide further information on arranging and seeking funding for suitably trained advocates (ideally with experience in ME/CFS) for people with ME/CFS, and acknowledge it takes time for them to get acquainted with the specifics of an individual's case to advocate effectively for them.	Thank you for your comment. It is not within the remit of NICE to make recommendations on the arrangements and funding for advocates.
Science for ME (S4ME)	Guideline	007	009 - 010	The guideline should provide further information on arranging and seeking funding for suitably trained advocates (ideally with experience in ME/CFS) for people with ME/CFS, and acknowledge it takes time for them to get acquainted with the specifics of an individual's case to advocate effectively for them.	Thank you for your comment. It is not within the remit of NICE to make recommendations on the arrangements and funding for advocates.
Science for ME (S4ME)	Guideline	007	008	This should be amended to include recognition that people with ME/CFS who need wheelchairs will need ones that fully recline, support the whole head and body, and be easily adjustable to change posture to minimise pain.	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	007	015	The term 'noise' should be replaced with the term 'sound' here and for every use of 'noise' in the guideline. 'Noise' suggests that	Thank you for your comment. This has been edited.

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				sound must be loud to a person of normal hearing to be problematic to a person with ME/CFS. This is not the case; quiet sound can be extremely difficult to tolerate for people with ME/CFS with severe sensitivity to sound.	
Science for ME (S4ME)	Guideline	007	016	After line 16, a further bullet point should be added for recognition of the sensitivities to sound and smells experienced by people with severe or very severe ME/CFS in all circumstances, including whenever communicating with or assisting the person with ME/CFS with activities of daily living.	Thank you for your comment. Hypersensitivity and the examples you mention are included in the previous recommendations on symptoms people with ME/CFS may experience.
Science for ME (S4ME)	Guideline	007	016	After line 16, a further bullet point should be added to include recognition that people with severe or very severe ME/CFS may need to remain in a horizontal or reclined position most or all of the time, and may require special equipment to enable this.	Thank you for your comment. This section highlights the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2, Evidence review C – access to care and the committee's experience. The committee acknowledge there are other symptoms that could be included and any list is not meant to be exhaustive. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care.
Science for ME (S4ME)	Guideline	008	005 - 009	We suggest addition of a bullet point in 1.2.2 stating the person with ME/CFS should keep an activity and symptom diary for review as part of this assessment. This should be compared with premorbid activity levels and may assist with the identification of PEM and so with a diagnosis.	Thank you for your comment. The committee decided at this stage, when suspecting ME/CFS, that asking people to keep an activity and symptom dairy is unnecessary and may worry people. This is further explored in the energy management section.
Science for ME (S4ME)	Guideline	008	008	Replace with: *'a psychological wellbeing assessment, if indicated or requested by the person with ME/CFS. Do not assume natural reactions to ME/CFS symptoms such as worry or changes in behaviour such as withdrawal from activities are indicators of mental health disorders.*' The term 'psychological wellbeing assessment' should be defined.	Thank you for your comment. The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness. At this stage the person has not been diagnosed with ME/CFS or any other condition and as you comment it is important to investigate the possibility of other diagnosis and co-existing conditions.

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					Psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing' to clarify this assessment.
Science for ME (S4ME)	Guideline	008	010	We suggest the criteria for suspecting ME/CFS could be clarified by providing information on common medical conditions that may result in a similar symptomatology, as this may aid physicians in ruling out such diagnoses and prevent mis-diagnosis with ME/CFS.	The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. In addition, the committee discuss misdiagnosis in the discussion section of Evidence review D- Diagnosis and include a list of differential diagnosis and conditions that commonly occur in people with ME/CFS.
Science for ME (S4ME)	Guideline	008	011	The word 'persistent' should be deleted due to similarity of 'persistent symptoms' to the term 'persistent physical symptoms' (PPS). The term PPS is often used interchangeably with 'medically unexplained symptoms' to describe physical symptoms for which an explanation has not yet been found, inappropriately implying there is no medical explanation to be uncovered and mental health issues are an underlying factor irrespective of whether they are actually present. Application of these terms may deter physicians from making appropriate referrals and investigations. Further, the wording 'the person has had all of the persistent symptoms' implies that all required symptoms must be present all the time for diagnosis to be made. PEM, by definition is an intermittent symptom related to activity level. Assuming it has to be 'persistent' may lead to missed diagnoses.	Thank you for your comment. The committee discussed the use of word persistent noting the sensitivities around the use of the word. However they agreed this was the best descriptor to use here in this context about symptoms as, 'continuing to exist or occur over a prolonged period'. This does not imply that all the symptoms need to be present all the time. The guideline provides clear recommendations advising physician when they should carry out investigations and make a referral.

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Science for ME (S4ME)	Guideline	008	016	Should include that specific onset typically follows an infectious illness. Should also acknowledge that some cases have gradual onset; not to specify this may exclude this subset from a diagnosis of ME/CFS, potentially leading to inappropriate management advice and harm to people with gradual onset ME/CFS. The IOM (Institute of Medicine) requirement for specific onset is qualified by 'not lifelong'.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. To note the committee doesn't assume the triggering event is an infective episode. The first recommendation in the guideline is, Be aware that ME/CFS is a ……… its pathophysiology remains under investigation'. In addition this text is in the context section, 'It is not clear what causes ME/CFS and the pathophysiology of ME/CFS remains under investigation. In many cases, symptoms are thought to have been triggered by an infection but it is not simple post-illness fatigue. It lasts longer and even minimal mental or physical activity can make symptoms worse.'
Science for ME (S4ME)	Guideline	008	017	(Box 1) Rather than giving an incomplete and misleadingly brief description of the core ME/CFS symptoms in Box 1, with hyperlinks to the definitions which may be ignored, it would be more helpful to provide the full definitions of each term at this crucial stage of the guideline where the terms are first introduced and need to be understood correctly for accurate diagnosis.	Thank you for your comments. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note more detailed definitions are given later and linked to for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	008	017	(Box 1) Fatigability and fatigue: The list of core symptoms, though based on the IOM (Institute of Medicine) criteria, has changed the first criterion from a description that clearly includes both fatigability (described as impairment to engage in former levels of activity) and fatigue, as two different features of the first criterion. We recommend adding	Thank you for your comments. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change fatigability. This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not

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				back fatigue, described as IOM does, as "often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest".	significantly relieved by rest.' The committee hope this has added some clarity for readers.
Science for ME (S4ME)	Guideline	008	017	(Box 1) PESE/PEM: The term Post-Exertional Symptom Exacerbation (PESE) should not be used. We support the continued use of the well recognised term 'post-exertional malaise' (PEM). There is a strong argument for including the word 'malaise' which has the specific medical meaning of feeling generally very unwell, and describes the experience of PEM well. Guidelines should work with widely accepted terms, rather than inventing new ones. PEM is the term used in international ME/CFS research and it is the term used in a wide range of training and information resources.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Science for ME (S4ME)	Guideline	008	017	(Box 1) Unrefreshing sleep: The bullet point on unrefreshing sleep should be revised. It is not clear what is meant by 'unrefreshing sleep'. The first subcategory of unrefreshing sleep lists symptoms experienced on waking; the second lists types of disordered sleep. It is not clear if symptoms on waking must be worse than normal to qualify as unrefreshing sleep, or if sleep not helping to resolve symptoms of ME/CFS is being mistaken for 'unrefreshing sleep'. Disordered sleep patterns may lead to increased symptoms on waking, but proper sleep does not lead to people with ME/CFS feeling better. 'Insomnia' should be included in 'broken or shallow sleep, altered sleep pattern or hypersomnia', as this is a significant symptoms for some people with ME/CFS.	Thank you for your comment. After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee have also edited the definition in the terms used in the guideline section. The committee hope this has added some clarity for readers.
Science for ME (S4ME)	Guideline	008	017	(Box 1) Cognitive difficulties: We are deeply concerned that cognitive difficulties are a requirement for suspecting ME/CFS in Box 1.	Thank you for your comment. The committee maintain that cognitive difficulties are a key symptom in suspecting ME/CFS and are commonly reported in people with ME/CFS. They note that cognitive difficulties (such as brain fog) are described in most of the criteria (7 of the 9)

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				This guideline recommendation is said to be based on the experience of the guideline committee (Evidence Review D, p.51 lines 26-28). The experience of a small committee is not an adequate basis for creating untested criteria. Promotion of cognitive difficulties to a requirement is a significant modification to IOM (Institute of Medicine) criteria, not a slight one (as claimed in Evidence Review D p.49 lines 44-45). It will significantly skew the balance of inclusion/exclusion towards exclusion, preventing a substantial subset of people who do not experience cognitive difficulties from obtaining a rightful diagnosis of ME/CFS, leading to inappropriate management advice and harms. We recommend that the IOM criteria should be followed in full, with the fourth listed required symptom being one of either cognitive difficulties or orthostatic intolerance. We would also agree to making the criteria for diagnosis less stringent by moving both cognitive difficulties and orthostatic intolerance to the list of other common symptoms. What we see no justification for, and harm resulting from, is the Committee's decision to make it mandatory for diagnosis that the person reports cognitive difficulties. We do not think it is right to exclude many people who meet internationally recognised ME/CFS criteria from being diagnosed with ME/CFS and getting the support and help they need. We are pleased to see a thorough description of cognitive difficulties with inclusion of subtypes and these should be retained in any amendment to cognitive difficulties in the criteria.	criteria) reviewed in Evidence review D in contrast with orthostatic intolerance (4 of the 9 criteria) supporting further their experience and expertise and this has been added to their discussion in the report.
Science for ME (S4ME)	Guideline	009	002 - 016	Should include a bullet point for gastrointestinal symptoms. Nausea is currently only addressed as a symptom of orthostatic intolerance.	Thank you for your comment. This has been added to the list of associated symptoms.

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Science for ME (S4ME)	Guideline	009	017 - 020	Members support an early provisional diagnosis but there was concern that patients be given information about the likelihood of recovery that is appropriate for the length of illness. Add: *'Ensure that any advice about the likelihood of recovery takes into account the time since onset: recovery rates are initially high but decrease to a lower level over the first two years of illness.'*	Thank you for your comment. Information on prognosis for people diagnosed with ME/CFS is included in section 1.6 information and support. The committee disagree that people with suspected ME/CFS should be given this specific information as they may not have a final diagnosis of ME/CFS.
Science for ME (S4ME)	Guideline	010	015 - 021	The advice to people with suspected ME/CFS to rest and not to use more energy than they perceive they have is good and should be retained. We suggest the term 'symptom-contingent pacing' be used throughout the guideline, to convey that activity levels should be judged on current symptoms with the object of avoiding post-exertional malaise.	Thank you for your comment. This section is about people with suspected ME/CFS and it is important that the advice recommended and terms used are also relevant to people that may have suspected ME/CFS but are in the end diagnosed with another condition. After considering stakeholders comments the committee edited the recommendations to simplify the wording and for this reason your suggestion has not been included. The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Science for ME (S4ME)	Guideline	010	001 - 003	Include recommendation for specialist input for all cases of suspected ME/CFS, since there is evidence of significant misdiagnosis in primary care.	Thank you for your comment. The following section on diagnosis recommends that after 3 months of symptoms people with suspected ME/CFS are referred to a ME/CFS specialist for the reasons that you comment on. See evidence review D- Diagnosis.
Science for ME (S4ME)	Guideline	010	017 - 019	Suggested alternative wording: '*Not to use more energy than a level that the person can sustain easily without leading to worsening symptoms, and not to continue increasing activity if symptoms begin to worsen.'* Reasoning: This avoids introducing new patients to a confusing metaphor (energy envelope).	Thank you for your comment. After considering the range of stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. At such keeping a diary at this stage may

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					not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
Science for ME (S4ME)	Guideline	010	022	People with suspected ME/CFS need to be given information about the likelihood of recovery that is appropriate for the length of their illness. Add to 1.3.2: '*Advise them that the likelihood of recovery decreases as time since onset increases; rates of full recovery are initially high but decrease to a lower level over the first two years of illness.*'	Thank you for your comment. Information on prognosis for people diagnosed with ME/CFS is included in section 1.6 information and support. The committee disagree that people with suspected ME/CFS should be given this specific information as they may not have a final diagnosis of ME/CFS.
Science for ME (S4ME)	Guideline	010	023	The word 'persistent' should be deleted due to similarity of 'persistent symptoms' to the term 'persistent physical symptoms' (PPS). The term PPS is often used interchangeably with 'medically unexplained symptoms' to describe physical symptoms for which an explanation has not yet been found, inappropriately implying there is no medical explanation to be uncovered and mental health issues are an underlying factor irrespective of whether they are actually present. Application of these terms may deter physicians from making appropriate referrals and investigations. Further, the wording 'diagnosis can only be confirmed after 3 months of persistent symptoms' implies that all required symptoms must be present all the time for diagnosis to be made. Post Exertional Malaise (PEM), by definition is an intermittent symptom related to activity level. Assuming it has to be 'persistent' may lead to missed diagnoses.	Thank you for your comment. The committee discussed the use of word persistent noting the sensitivities around the use of the word. However they agreed this was the best descriptor to use here in this context about symptoms as, 'continuing to exist or occur over a prolonged period'. This does not imply that all the symptoms need to be present all the time. The guideline provides clear recommendations advising physician when they should carry out investigations and make a referral.
Science for ME (S4ME)	Guideline	011	009 - 012	Not every young person will want a management plan (medical care plan), be able to travel to see a specialist team, or even be able to participate in an evaluation in their own home.	Thank you for your comment.

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				Replace with: '*After provisional diagnosis, with the agreement of the child with ME/CFS and their family, or the young person with ME/CFS, refer them to a paediatrician working in a relevant biomedical discipline who has specialist knowledge of ME/CFS in accordance with this guideline to confirm diagnosis and develop a medical care plan (management plan).*'	The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan Access to services The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and as we note above your suggestions for additions to the recommendation are reinforced throughout the guideline for this reason your suggestion has not been added.
Science for ME (S4ME)	Guideline	011	005 - 006	Include that diagnosis should ideally be made by a specialist physician who has up-to-date knowledge of ME/CFS in keeping with this guideline, but acknowledge that the person may not be able to travel to a specialist service for diagnosis, and diagnosis by GP with input from a specialist physician may be appropriate in such cases.	Thank you for your comment. Based on the evidence (see XXX) and in the committee's experience clinicians working within a ME/CFS specialist team are the best healthcare professionals to confirm diagnosis and develop a care and support plan, they have the expertise in

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					ME/CFS and the understanding of the detailed assessment required at this stage. For this reason the committee have recommended that diagnosis and the development of the care and support plan should be carried out by a ME/CFS specialist team. Any clinician not working in collaboration with and supported by a ME/CFS specialist team should not be developing the care and support plan. The committee agree that review of the care and support plan can take place in primary care and this is set out in the review in primary care section of the guideline. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. In addition the access to services section of the guideline recommends that the timing, length and frequency of appointment should be adapted to the person's needs.
Science for ME (S4ME)	Guideline	011	005 - 006	We agree with early provisional diagnosis. We suggest this recommendation include that investigations should be continued after diagnosis to rule out other possible conditions. A single referral may have a wait time of more than three months, but management in accordance with this guideline should not be delayed if ME/CFS is suspected. *Add: 'Management in accordance with this guideline should not be delayed if ME/CFS is suspected, even if investigations to rule out other conditions continue.'*	Thank you for your comment. In the section on suspecting ME/CFS the committee have recommended carrying out any tests where ME/CFS is suspected to exclude or identify other diagnoses and emphasise the importance of clinical judgment when deciding on tests. The committee note that it is the ME/CFS specialist team that confirm the diagnosis.

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					After considering the stakeholder comments the committee have added a recommendation in the diagnosis section reinforcing the importance of seeking advice if there is any uncertainty in interpreting signs and symptoms and whether further investigations are needed. The committee agree that early support with the management of symptoms could be helpful and have made recommendations on this. Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for advice for people with suspected ME/CFS. They note there is a lack of trial evidence to support specific advice for people with suspected ME/CFS but the committee agreed the advice they have recommended would not be harmful in the short term. The committee recommend a personalised approach and this would include discussing with the person with suspected ME/CFS about how to manage their symptoms.
Science for ME (S4ME)	Guideline	011	007 - 008	Replace with: *'After a primary care provisional diagnosis,* refer *the person to a consultant working in a relevant biomedical discipline who has specialist knowledge of ME/CFS in accordance with this guideline to carry out any further tests needed to confirm the diagnosis. If the patient agrees, the consultant led team should develop a management plan (medical care plan) with the patient. In severe cases this may require a home visit or other special arrangements.'*	Thank you for your comment. The committee agreed that as the recommendation refers to ME/CFS specialist team this includes sufficient referral detail. The committee have added a definition of a ME/CFS specialist team in the terms used in the guideline. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan. Management plan has been edited to 'care and support plan' in line with personalised care and support plans

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					https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The committee hope this adds further clarity and for the reasons set out above your suggestion has not been added.
Science for ME (S4ME)	Guideline	011	015 - 016	Why is there an additional requirement for a 'holistic assessment' after diagnosis is made? A proper diagnostic process should include taking a full history and conducting physical exams. Performing a 'holistic assessment' in addition means duplication of history-taking, physical exams and assessments, which may be difficult for people with ME/CFS to achieve and may cause worsening.	Thank you for your comment. This assessment takes place after referral to a ME/CFS specialist team. In the committee discussion in Evidence review I- multidisciplinary care set out the importance of this assessment in confirming the diagnosis and in developing the personalised care and support plan. Feedback from stakeholders and experience from the committee indicates that GPs did not have enough time to carry out the assessments needed to confirm a diagnosis of ME/CFS or to develop a care and support plan in a single standard appointment. *Access to services* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the guideline home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. In addition the access to services section of the guideline recommends that the timing, length and frequency of appointment should be adapted to the person's needs.
Science for ME (S4ME)	Guideline	011	003	We suggest a list of common conditions that should be excluded as part of the diagnostic process and a list of tests that should be carried out be specified, so that GPs have guidance on this for cases where specialist referral is not possible.	Thank you for your comment. The committee agree it is important to exclude other diagnoses and recommended that where ME/CFS is suspected investigations should be carried out to exclude other diagnoses. After considering the stakeholder comments about the lack of

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					prominence and clarity around the exclusion of other diagnoses the committee have added examples of investigations to be done when suspecting ME/CFS and have added that ME/CFS should be suspected if the 'symptoms are not explained by another condition.' The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS.
Science for ME (S4ME)	Guideline	011	006	Wording 'persisted for' implies that symptoms must have been present all the time for diagnosis to be made. Inclusion of this wording may lead to failure to diagnose ME/CFS for many.	Thank you for your comment. The committee discussed the use of word persistent noting the sensitivities around the use of the word. However they agreed this was the best descriptor to use here in this context about symptoms as, 'continuing to exist or occur over a prolonged period'. This does not imply that all the symptoms need to be present all the time. The guideline provides clear recommendations advising physician when they should carry out investigations and make a referral.
Science for ME (S4ME)	Guideline	011	013	There should be a clear statement in section 1.5 that people with ME/CFS should not be referred to MUS or fatigue clinics for assessment and care planning or at any other stage in the diagnosis, assessment and care of ME/CFS, as these clinics do not specialise in ME/CFS and may take an inappropriate approach which does not adequately take considerations specific to ME/CFS into account. People with ME/CFS should only be referred to pain clinics that have an up-to-date understanding of ME/CFS in keeping with this guideline.	Thank you for your comment. The guideline is clear that referral is to a ME/CFS specialist team and it is not necessary to include where people should not be referred to. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.
Science for ME (S4ME)	Guideline	011	015	The guideline should suggest that input for original development of a management plan (medical care plan) should be taken from recent medical notes where possible. Information should be gathered by modes of communication accessible for the person with ME/CFS, e.g., by email, or correspondence by post, enabling them to respond at their own pace. If face-to-face visits are required to enable this home visits should be offered for the	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly

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				moderate, severe and very severe. We also suggest linking to 1.8 'Access to care' in 1.5.1.	challenging. As you note this is identified in the access to care section and in the section for people with severe and very severe ME/CFS. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note this point is made in the guideline and for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	011	015	It should be specified that this assessment should only be carried out by a physician with up-to-date knowledge of ME/CFS in keeping with this guideline.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	011	015	The word 'holistic' should be deleted. It is commonly associated with alternative medicine.	Thank you for your comment. A holistic assessment is an assessment that looks at the whole person not just a person's condition. This approach supports personalised care and support planning where a plan is developed after an initial holistic assessment (https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.

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Science for ME (S4ME)	Guideline	012	001 - 002	The words, *'and other causes of physical or emotional stress'* should be deleted. This is already covered by '*anything known to exacerbate symptoms*', so duplicates content. Deletion may also reduce risk of misinterpretation that 'stress' may be a cause or perpetuating factor of ME/CFS.	Thank you for your comment. This has been deleted.
Science for ME (S4ME)	Guideline	012	025 - 026	The recommendations referred to as covering symptom management should read '1.11.24-1.11.42' (and not 1.11.27-1.11.50 as they do presently). This would correctly cover the section on 'Managing orthostatic intolerance', which is currently excluded from the range given, and would also correctly remove reference to the section on 'Psychological support', as psychological support should not be offered to manage symptoms of ME/CFS.	Thank you for your comment. The links have been updated.
Science for ME (S4ME)	Guideline	012	004	The word 'psychosocial' should be deleted. The wording, '*The impact of symptoms on wellbeing*' is adequate. 'Psychosocial' is a loaded term in the context of ME/CFS. We do not think that formal psychological assessment is relevant unless it is requested or indicated.	Thank you for your comment. After considering the range of stakeholder comments, this bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing'. As with all medical assessments clinical judgement should be used and appropriate to the person having the assessment.
Science for ME (S4ME)	Guideline	012	010	It should be specified in 1.5.2 that the 'management plan' should be developed by a GP, consultant physician, or specialist nurse who is part of the consultant's team, and they should have up-to-date ME/CFS training in accordance with this guideline. There should be recommendation for ongoing specialist oversight where available but with acknowledgment some people with ME/CFS may prefer or only be able to access assessment and care planning by their GP. People with ME/CFS under a consultant should not be discharged back to their GPs unless requested, to enable continuity of care and prevent repeat re-referral. The guideline should also specify that the person with ME/CFS should have a named contact (per recommendation 1.10.3) who will ideally be a specialist nurse (and not a therapist) with up-to-date training in ME/CFS consistent with this guideline and be the person with ME/CFS should be informed how to contact them.	Thank you for your comment. This section is assessment and care and support planning by a ME/CFS specialist team. It is the ME/CFS specialist team that confirm the diagnosis and develop the care and support plan. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. The review in primary care section of the guideline recommends a review of the care and support plan at least once a year.

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					As you note the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Science for ME (S4ME)	Guideline	012	010	We consider the term 'medical care plan' to be more appropriate than 'management plan'. The former makes it clear that it is a plan to deliver care. The term 'management plan' implies that the person with ME/CFS and their condition are to be managed. All uses of 'management plan' throughout the draft guideline should be changed to 'medical care plan'.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Science for ME (S4ME)	Guideline	013	016 - 018	'individual or group peer support' may be added to the list of example formats. Our members find interacting with other people with ME/CFS (whether in person or online) a useful means of learning how to cope with the condition.	Thank you for your comment. This recommendation refers to the format of information. Later in this section support groups are mentioned.
Science for ME (S4ME)	Guideline	013	009 - 010	We suggest inclusion of the words '*the person with ME/CFS should be kept informed at all stages of assessment for and*	Thank you for your comment. This recommendation is about the communication of the care and support plan. The recommendation above is clear that the

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				development of the management plan (medical care plan) and be provided with copies of written records of these'.	person is charge and their care and support plan. Throughout the guideline the committee have reinforced the principle of collaborative care and good communication. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. These points are made in the guideline and for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	013	012 - 013	1.5.5 should include that home visits to collect large amounts of information from people with severe or very severe ME/CFS are unlikely to be successful or safe. Almost all people with ME/CFS would benefit from being given the questions online or in hard copy so they can be completed at their own pace. We also suggest inclusion of a link at 1.5.5 to 1.8 'Access to care'.	Thank you for your comment. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. To note after considering the stakeholder comments the committee agreed to bring the recommendations on people with severe and very severe ME/CFS together in one section to ensure their particular needs were not hidden within the guideline. In the context of home visits, this recommendation on offering home visits is now followed by the recommendation on providing flexible access. The committee agreed it is important that people are offered home visits for the assessment and development of the care and support plan but other methods may be more appropriate depending on the person's symptoms.

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Science for ME (S4ME)	Guideline	013	002	The words '*The plan should be mutually agreed*' should be deleted. It may contradict the earlier clause '*the person with ME/CFS is in charge of the aims of their management plan*'. Healthcare workers may have unrealistic ideas about what activity levels and types the person with ME/CFS can cope with, meaning development of unsustainable management plans which may result in harm to people with ME/CFS.	Thank you for your comment. This has been deleted.
Science for ME (S4ME)	Guideline	013	013	The word 'holistic' should be deleted. It is commonly associated with alternative medicine.	Thank you for your comment. A holistic assessment is an assessment that looks at the whole person not just a person's condition. This approach support personalised care and support planning where a plan is developed after an initial holistic assessment (https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.
Science for ME (S4ME)	Guideline	013	014	We appreciate that section 1.6 sets out the major impact of the illness on the lives of people with ME/CFS and makes it clear how important accurate and up-to-date information on financial and social support for people with ME/CFS and their families and carers are.	Thank you for your comment.
Science for ME (S4ME)	Guideline	014	009 - 014	We strongly agree information provided to people with ME/CFS and their families/carers should be up-to-date. However, it should also be stated that it must be in accordance with this guideline. It should not be about 'chronic fatigue', or medically unexplained symptoms (MUS), or based on excessively broad diagnostic criteria that excludes post-exertional malaise as a requirement for diagnosis. It should not suggest recovery can be achieved by exercise, increasing activity, changing behaviours or beliefs about the illness, or better stress management. It should not present speculation on cause of ME/CFS as fact.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. See evidence review B – information for health and social care professionals for the evidence and committee discussion on this topic.
Science for ME (S4ME)	Guideline	014	009 - 014	Add: '*ME/CFS information prepared prior to this guideline must be reviewed and, if necessary, re-written to ensure compliance with this guideline before it is distributed*'.	Thank you for your comment. Recommending the review of material is not within the remit of NICE.

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					The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Science for ME (S4ME)	Guideline	014	016 - 018	Clarify that while symptoms may fluctuate, overall severity status may deteriorate significantly and rapidly, but overall improvement (when this does take place) usually happens gradually over much longer time periods.	Thank you for your comment. The long term outlook and variation in impact is covered in the next part of the recommendation.
Science for ME (S4ME)	Guideline	014	019 - 021	Delete, as repeats content at lines 16-18 and 22-24. Alternatively, replace 'often' with 'may' and remission should be qualified with 'partial' to clarify that remission may not mean complete remission. I.e., '*may involve periods of partial remission and relapse or prolonged deterioration*'. Although the condition can fluctuate, our members report that periods of complete remission are rare, so the current phrasing could be misleading.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited these bullet points and hope this addresses your points: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Science for ME (S4ME)	Guideline	014	022 - 024	This statement is not correct given that diagnoses are being given before 6 months. Discussion of prognosis for adults and children would be best covered in the same recommendation. Replace with: '*varies in long-term outlook from person to person. Recovery rates decrease with increasing lengths of illness. Recovery rates are initially high but full recovery is rare after two years. The outlook for children and young people tends to be better than in adults*.'	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS

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Science for ME (S4ME)	Guideline	014	026 - 027	Should replace 'may' with 'will', i.e., '*will need to adjust how they live*'. The use of 'may' underplays the effect of even mild ME, which by diagnostic definition significantly reduces the ability to carry out daily activities. We suggest adding: '*Many people with ME/CFS will need to make significant adjustments to or discontinue their current work or educational commitments.*'	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet points and hope this addresses your point: • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Science for ME (S4ME)	Guideline	014	028 - 029	Lines 28-29 should be deleted. ME/CFS is worsened by cumulative energy expenditure in excess of what can be tolerated. It is therefore incorrect to refer to specific triggers. We are not aware of reliable evidence that childbirth causes a worsening of ME/CFS greater than any similar exertion might, and some women report an improvement during pregnancy or after giving birth.	Thank you for your comment. There were several stakeholder comments about the examples of triggers that worsen ME/CFS. Some of the examples as suggested in your comment were considered potentially misleading information and not always a trigger and there are comments that gave other examples that could be added. After considering the stakeholder comments the committee agreed to delete the examples and not provide any examples in the recommendation recognising the variation in triggers in people with ME/CFS.
Science for ME (S4ME)	Guideline	014	030 - 031	The words 'may be self-managed with support and advice' underplays the seriousness of the illness. People with very severe ME/CFS may be completely reliant on others. Replace with: '*has no cure or effective treatments. Energy management (including symptom-contingent pacing) may help to reduce the impact of symptoms*.'	Thank you for your comment. The committee disagree these words underplay the seriousness of ME/CFS, the previous bullet points are clear about the range of impact in people with ME/CFS.
Science for ME (S4ME)	Guideline	014	016	Delete: 'that affects everyone differently'. This is true for all medical conditions. Highlighting it here suggests more variability than is the case and may lead to misdiagnoses. Diagnosis requires meeting specific criteria (section 1.2).	Thank you for your comment. The committee disagree, it is accepted that ME/CFS does impact people differently and there is a wide range of impact in how its affects people's lives. This is supported by the qualitative evidence in evidence reviews A and B and their experience for this reason your suggested edit has not been made.
Science for ME (S4ME)	Guideline	014	025	Should replace 'can have' with 'has', i.e., '*has a major impact on people's lives*', as ME/CFS always has a major impact on people's lives.	Thank you for your comment.

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					After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe).
Science for ME (S4ME)	Guideline	014	031	Add a bullet point in 1.6.4 to explain that ME/CFS can be worsened by over-exertion and that it is important for the person with ME/CFS to avoid over-exertion for this reason.	Thank you for your comment. This recommendation is to give an overview of ME/CFS and there is more detail throughout the guideline on aspects of ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made later in the energy management section of the guideline and for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	015	001 - 003	Discussion of prognosis for adults and children would be best covered in the same recommendation. Replace with: '*varies in long-term outlook from person to person. Recovery rates decrease with increasing lengths of illness. Recovery rates are initially high but full recovery is rare after two years. The outlook for children and young people tends to be better than for adults.'*	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS. The following recommendation explains that the outlook for children and young people is better than in adults.
Science for ME (S4ME)	Guideline	015	016 - 018	After 1.6.9, add a new recommendation: '*With the consent of the person with ME/CFS, provide information to care agencies about the severity of their symptoms and their specific needs*.'	Thank you for your comment. This section is about how to access social care and not about the communication of information between services and for this reason your suggestion has not been added.

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Science for ME (S4ME)	Guideline	015	008	After 1.6.6, add a new recommendation: '*provide appropriate letters and reports to benefits and insurance agencies in support of unemployment and disability benefits and claims. Ensure patients have been recently reviewed so such reports are up to date*.'	Thank you for your comment. The committee agree that signposting to benefits is important but were not able to make recommendations on the documentation that should be provided and who it should be provided to.
Science for ME (S4ME)	Guideline	016	012 - 015	It should be recommended that in the best interests of the person with ME/CFS, where possible, a health or social care professional chosen by the person with ME/CFS be involved in any such assessment.	Thank you for your comment. These assessments are formal processes and it is not in the remit of this guideline to make recommendations about who the person can choose to be involved.
Science for ME (S4ME)	Guideline	016	012 - 015	Include ensuring that where possible, the person with ME/CFS should have a family member or advocate present for any such assessment.	Thank you for your comment. These assessments are formal processes and it is not in the remit of this guideline to make recommendations about who the person can choose to be involved.
Science for ME (S4ME)	Guideline	016	012 - 015	Add that health and social care professionals should only have involvement if they understand that ME/CFS is not a psychiatric disorder and that it is not appropriate to reframe the symptoms of ME/CFS as another condition.	Thank you for your comment. These assessments are formal processes and it is not in the remit of this guideline to add this suggestion.
Science for ME (S4ME)	Guideline	016	012 - 015	Specify that 'training and experience in ME/CFS' must be up-to-date and consistent with this guideline, as inadequately informed health and social care workers may do enormous harm.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. 'up-to-date' does not add any further clarity to the recommendation and for this reason your suggestion has not been added. .
Science for ME (S4ME)	Guideline	016	006 - 008	Add at the beginning of the recommendation: 'Considerable harm has been caused by mistaking ME/CFS as mental illness, abuse or neglect'. Specify that training and experience should be in accordance with the recommendations in this guideline. Older training and previous experience may be out of date and lead to	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the

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				inaccurate assessments and significant harm to people with ME/CFS..	recommendations in the training for health and social care professionals section of the guideline. With regard to safeguarding the importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.
Science for ME (S4ME)	Guideline	016	006 - 008	The sentence 'Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS' can be misread as suggesting everyone with ME/CFS needs a safeguarding assessment. We recommend adding to the beginning of the sentence: 'If abuse or neglect is suspected, ... '	Thank you for your comment. This recommendation has been edited to, 'If a person with confirmed or suspected ME/CFS needs a safeguarding assessment directly involve a health and social care professionals who have training and experience in ME/CFS. The committee hopes this adds some clarity for readers.
Science for ME (S4ME)	Guideline	016	009 - 011	Replace with this: 'Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of mental illness (including eating disorders) or of abuse or neglect.' We recommend moving section 1.7.2 to before section 1.7.1 to emphasise that this section is about the problems of symptoms of ME/CFS being misinterpreted as safeguarding issues.	Thank you for your comment. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'.
Science for ME (S4ME)	Guideline	016	005	General comment for safeguarding section Move the content of 1.7 Safeguarding ME/CFS to the Section 1.2 Suspecting ME/CFS. The reason safeguarding requires comment in this guideline is because there have been failures on the part of doctors to recognise ME/CFS, and to convey that diagnosis and the implications of it clearly to social services. Therefore, it is an issue of needing to take great care when considering differential diagnoses of mental illness or parental abuse or neglect. The currently separate section on safeguarding may actually contribute to the incorrect suggestion that	Thank you for your comment. After considering the stakeholder comments this section has been reordered and the now second recommendation has been edited to,' *If* a person with confirmed or suspected ME/CFS needs to be assessed'. When considering the stakeholder comments and the structure of the guideline the committee agreed that the safeguarding section was already appropriately placed.

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				safeguarding is more likely to be required in ME/CFS than in other chronic illnesses.	
Science for ME (S4ME)	Guideline	016	005	We appreciate the clear statements in 1.7 that professionals involved in safeguarding should have experience in ME/CFS, that symptoms of severe or very severe ME/CFS may be confused with signs of abuse or neglect, and that response to possible child abuse and neglect should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability.	Thank you for your comment.
Science for ME (S4ME)	Guideline	016	005	There will need to be substantial retraining of health and social care professionals involved in safeguarding processes for people with ME/CFS. Such training should be in accordance with the recommendations in this guideline.	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. This applies to this section.
Science for ME (S4ME)	Guideline	017	008 - 019	We recommend moving section 1.7.6 to the beginning of the 'children and young people' section, before section 1.7.4. This would help to emphasise that the issue being addressed is misunderstanding of symptoms leading to inappropriate diagnosis of FII and other safeguarding issues.	Thank you for your comment. After considering the stakeholder comments these recommendations have been reordered.
Science for ME (S4ME)	Guideline	017	014 - 016	Should also cover refusal of assessment for and development of the management plan or declining to restart any part of it. Suggested wording: '*declining assessment for and development of a management plan (medical care plan), or disagreeing with, declining, withdrawing from or refusing to restart any part of their management plan (medical care plan), either by the child or young person, or by their parents or carers on their behalf*'	Thank you for your comment. Recommendation 1.15 in the principles for care section of the guideline addresses the points you make. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	017	019	Should include not participating in home schooling.	Thank you for your comment. This covered by the general point about reduced or on-attendance at school. Evidence review B has further detail on the

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					committee discussion about safeguarding and schooling or reduced activities.
Science for ME (S4ME)	Guideline	017	020	Access to Care: Overall section 1.8 is helpful. We are concerned that there will be a wide gap between what is recommended and what happens in practice. We recommend that the importance of this section be emphasised in the guideline. Many people with ME/CFS currently have no access to current medical services, not just for their ME/CFS symptoms, but for other serious comorbidities and even for emergencies, because of insurmountable barriers to access.	Thank you for your comment.
Science for ME (S4ME)	Guideline	017	020	Add: We recommend that an NHS endorsed ME/CFS passport be developed that sets out the requirements of the individual patient during health care interactions. Information about the patient's requirements should be included in their medical notes and made clear to all clinical and hospital staff who deal with them.	Thank you for your comment. Documentation Types of documentation was not prioritised for review and the committee were unable to make further recommendations on documentation and have not added Patient Healthcare passports but the committee recognise the importance of people having copies of their care and support plan and have recommended this in the assessment and care support planning section of the guideline. In addition after considering stakeholder comments the management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Science for ME (S4ME)	Guideline	017	021	'people with ME/CFS...' Add: 'and those awaiting possible ME/CFS diagnosis'.	Thank you for your comment. This section is about access to care for people with a confirmed diagnosis of ME/CFS. While the committee agree that many of the recommendations could apply to any one accessing services there are recommendations that are specific to people with ME/CFS for this reason your suggestion has not been added.

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Science for ME (S4ME)	Guideline	018	008 - 009	care flexibility: Add email, and letter as options. Add providing a quiet, dimmable separate place to lie down, and option to wait in car, while awaiting appointment. Make it clear that this applies for all severity levels of ME/CFS. Add: People with ME/CFS who live alone and have no car may need assistance with arranging safe and manageable transport to and from appointments, or home visits.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. Unless otherwise stated the recommendations in the guideline apply to all people with ME/CFS. A statement has been added to the beginning of the recommendations to clarify this.
Science for ME (S4ME)	Guideline	018	001	Add: 'discussing any proposed referral with the person with ME/CFS before making it and considering related access needs'	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.
Science for ME (S4ME)	Guideline	018	006	replace 'noise' with 'sound (speak quietly)' It is not just loud sound that affects people with ME/CFS.	Thank you for your comment. Noise has been replaced with sound.
Science for ME (S4ME)	Guideline	018	009	Add 'be aware of the patient's cognitive problems and physical fatigability during consultations. Make accommodations for this, for example by making use of written and electronic communication before and after a consultation. Allow patients to bring notes prepared in advance to be entered in their medical records. For patients with severe ME/CFS and others who request it, provide a written summary of all consultations.'	Thank you for your comment. The symptoms that people with ME/CFS experience and their impact is described elsewhere in the guideline (for example, the suspecting ME/CFS section) and this section to address those difficulties. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.

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Science for ME (S4ME)	Guideline	018	015	change 'fear of relapse' to 'likelihood of triggering PEM or deterioration', as 'fears' are likely to be rational and founded in experience (see Evidence Review G, p.326, lines 45-47).	Thank you for your comment. After considering stakeholder comments about the word fear this recommendation has been edited 'risk that their symptoms will worsen may prevent people from leaving their home'.
Science for ME (S4ME)	Guideline	018	018	Add an extra bullet point: 'The person is likely to have prepared with pre-emptive rest in order to be able to attend an appointment.'	Thank you for your comment. This recommendation raises awareness about the reasons people may miss an appointment not about preparation for an appointment and for that reason your suggestion has not been added.
Science for ME (S4ME)	Guideline	018	019	People with severe or very severe ME/CFS This section should also be applied to people with moderate ME/CFS who are largely housebound and have similar problems with access to and use of services.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS and the first recommendation in this section addresses this.
Science for ME (S4ME)	Guideline	018	023	add: communication with a carer on the person with ME/CFS's behalf (with their agreement). add: communications that are not real-time (such as texts and emails) may be particularly useful for this group.	Thank you for your comment. The section on awareness of severe or very severe ME/CFS and its impact includes information on supporting communication with an advocate. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for these reason your suggestions has not been added to the recommendation.
Science for ME (S4ME)	Guideline	019	021 - 029	This section needs to make it clear that ordinary minor stimuli may be very painful and may lead to prolonged symptom worsening. line 25: add: 'and being aware that physical examinations, tests and scans can cause severe pain or deterioration. Ensure the	Thank you for your comment. These are examples of what to consider in facilitating a low stimulus environment in a hospital, it is not meant to be exhaustive and for this reason your suggestions have not been added.

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				patient is listened to and provide any needed accommodations, sedation or pain relief. line 26: 'lights dimmed' add 'and off whenever possible'. line 27: Change 'noise' to 'sound' line 29: Change 'strong smells' to 'smells'.	Sound has been replaced with noise.
Science for ME (S4ME)	Guideline	019	013 - 016	add: where needed arrange ambulance travel to and from hospital or hospital stretcher between car and ward.	Thank you for your comment. Examples supporting transfer to hospital are given but these are not meant to be exhaustive for this reason your suggestion has not been added to the recommendation. This has been added to the discussion section of Evidence review C- Access to care.
Science for ME (S4ME)	Guideline	019	007	replace 'noise' with 'sound', as even quiet sounds may be a problem for some people with ME/CFS.	Thank you for your comment. Noise has been replaced with sound.
Science for ME (S4ME)	Guideline	019	019	Add bullet points to Section 1.8.6: - 'minimise disruption to the patient's sleep, where possible accommodate the patient's sleep schedule. - Ensure nursing and other appropriate staff are apprised of needs re assistance with washing, toileting, and feeding when required. Some people with ME/CFS without having the outward appearance of needing support, may need assistance.	Thank you for your comment. These are examples of what to consider in facilitating a low stimulus environment in a hospital, it is not meant to be exhaustive and for this reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	019	020	'aim to provide a single room where possible' is not sufficient. People with severe or very severe ME/CFS are likely to deteriorate in a hospital ward. For these people, a single room is not a 'nice to have' but a need; they are likely to choose not to be in hospital if their need for a quiet low-stimulus room cannot be met. Add: people with very severe ME may be unable to communicate their needs, with hospital staff. Provision should be made for their carer to stay with them in hospital to assist staff in ensuring care is provided to minimise symptom exacerbation.	Thank you for your comment. The committee recognise the importance of people with severe or very severe ME/CFS having a low stimulus environment in hospital and this includes a single room but they also recognised there may be occasions where this is not possible. The section on awareness of severe or very severe ME/CFS and its impact includes information on supporting communication with an advocate. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestions have not been added to the recommendation.

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Science for ME (S4ME)	Guideline	020	020 - 022	Add: For patients who don't yet have a management plan (medical care plan), do not delay access to aids and appliances until the plan is completed.	Thank you for your comment.
Science for ME (S4ME)	Guideline	020	006 - 007	'access to outside space' Some people with ME/CFS may have great difficulty accessing public spaces due to the impact of sounds and social contact, and so a private outside space such as a garden may be important for well-being and health maintenance e.g. exposure to sunlight.	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised.
Science for ME (S4ME)	Guideline	020	017 - 018	'families and carers ...' Add: 'and care agencies and their staff' It should not be assumed that people with ME/CFS have families or consistent carers. Add: The medical team should liaise with social services and care agencies to ensure they have up to date written information on the individual's care needs, including extra time needed for some care tasks. Add: Ensure the person with severe or very severe ME has access to appropriately trained advocacy services to help them access the medical, care, practical support and financial support they need. Add: Consider, where appropriate, referral for respite care or palliative care services. In very severe cases it may be appropriate to consult a palliative care specialist.	Thank you for your comment. This recommendation refers directly to families and unpaid carers and this is clarified in the terms used in the guidance.
Science for ME (S4ME)	Guideline	020	029 - 030	delete 'taking into account risks and benefits'. An evaluation of risks and benefits should be done for any recommendation for aids and adaptations, but its explicit mention here seems to reinforce the mistaken view that the use of aids can lead to a reduced incentive to be active.	Thank you for your comment. The committee agree there are risks and benefits to all strategies to support people with ME/CFS managing their symptoms and any risk, if any, will be individual to the person and should be discussed. For this reason this hasn't been deleted.
Science for ME (S4ME)	Guideline	020	009	'glare from lights' change to 'reduce light levels'.	Thank you for your comment. This change has been made.

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Science for ME (S4ME)	Guideline	020	010	'loud noise' change to 'sound at levels that cause them problems' Add 'Exposure to sensory stimuli, at levels healthy people can easily tolerate, is not only difficult to cope with at the time, but can lead to rapid physical and/or cognitive deterioration.'	Thank you for your comments. Sound levels has been added. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.
Science for ME (S4ME)	Guideline	020	011	Add: Accommodation not at ground level will usually present difficulties for people with ME/CFS, particularly for people using wheelchairs, and especially reclining wheelchairs. Even if lifts are large enough, sounds and vibrations can be troublesome for people with severe sensitivities and may not be available during an emergency evacuation.	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.
Science for ME (S4ME)	Guideline	020	030	Add: Orthostatic intolerance may mean that some people with ME/CFS require fully tilting and reclining wheelchairs and chairs.	Thank you for your comment These are examples in the recommendation and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	021	011 - 014	Not all patients have, are able to get, or want, management plans. Not all information in a management plan should be shared with an employer, school or support service. Information provided to third parties needs to be limited to that which is directly relevant. Replace with '*Offer to liaise on the person's behalf (with their informed consent) with employers, education providers and support services. Give them information about ME/CFS, and relevant aspects of the person's illness, including any adjustments required*.' Add bullet points to 1.9.2: - '*Ensure the person with ME/CFS is included in all decision making with employers, apprised of the content of all discussion, and provided with copies of all correspondence relating to them.*' - '*communications between a person's employer or education provider, health and social care professionals, and training and*	Thank you for your comment. The committee agree that the issue of choice and consent is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan. Taking this into account no edits have been made to the recommendation.

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				education services must respect patient confidentiality and comply with relevant data protection law at all times'	
Science for ME (S4ME)	Guideline	021	004 - 005	Many people with ME/CFS will not be able to return to work or education at all, or may gradually deteriorate due to doing more than can be sustained. Therefore the advice needs to be realistic. People with ME/CFS need to be made aware that recovery is most likely in the first two years. After that time, there is only a very small probability of a full recovery and plans to return to work may be unrealistic. Clarity about this will help the patient and their family plan appropriately. Add bullet point to 1.9.1: *- 'Ensure the person has information on how to access advice on the financial implications of, and their rights in relation to, changes to employment arrangements including stopping and starting work, and reducing hours.'*	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. The social care and maintaining independence sections of the guideline provide information about accessing benefits.
Science for ME (S4ME)	Guideline	022	003 - 005	Add 3 bullets points to 1.9.4: *- 'The child or young person's health needs to take priority over education, and there may be times when it is best to step away from education to allow the child to rest without pressure of trying to keep up with work. Flexibility needs to include complete breaks during times of severe illness.'* - '*When relevant, health and social care professionals should explain to training and education services that some children and young people with ME/CFS are not only unable to attend school but may have significantly reduced ability to engage in online or home schooling, or may need to discontinue schooling of any form altogether on either a short or long-term basis.*' *- 'Ensure the young person with ME/CFS is included in all decision making with education providers, apprised of the content of all discussion, and provided with copies of all correspondence relating to them.'*	Thank you for your comment. Further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion and for this reason have not been added to the recommendation.

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Science for ME (S4ME)	Guideline	022	010 - 012	This is both too prescriptive and unrealistic. Suggested replacement version: *'Advise children and young people with ME/CFS (and their parents and carers) that:* *- The first priority should be to avoid any deterioration of health while achieving some quality of life* *- they should be free to choose which aspects of education, home and family life and social activities they prefer to spend their very limited energy on, without pressure to conform to social norms expected of heathy children. For some this may mean withdrawing from education. There should be no pressure to return to education until their health allows* *- recognise cognitive problems that are part of ME/CFS may make some subjects too difficult for the child to study. Flexibility on subject choices is important.'*	Thank you for your comment. The committee disagree this is too prescriptive it is a broad recommendation that advises about balancing activities. The detail of the balance will depend on the child or the young person. For this reason your suggestion has not been added.
Science for ME (S4ME)	Guideline	022	001 - 002	We are concerned about the statement 'discuss the child or young person's management plan'. This may include information not appropriately shared with people other than their medical team. Only relevant parts should be discussed, and only with informed consent.	Thank you for your comment. The committee agree that the issue of choice and consent is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and what information is shared with their consent.
Science for ME (S4ME)	Guideline	022	013	Section 1.10 Multidisciplinary care – Overall Comment We suggest changing the heading of section 1.10 from	Thank you for your comment.

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				'Multidisciplinary care' to 'Coordination of care', as referred to in Evidence Review I (p.23 line 46) and to reflect use in the NICE clinical guideline, 'Multiple sclerosis in adults: management' (CG186). The current section 1.10 heading is misleading as it implies all people with ME/CFS need multidisciplinary care. Many people with ME/CFS will neither need nor want multidisciplinary care, having no need for physiotherapy, occupational therapy, psychological therapy or dietary advice. Many will be well served by consultant diagnosis, and ongoing help and review as needed by a specialist nurse and GP. We are pleased the committee has recognised the importance of a single point of contact to coordinate care for people with ME/CFS in order to mitigate the risk of contact and appointments with several different people impacting *'negatively on the person's health potentially worsening symptoms'* (Evidence Review I p.21 lines 26-29; pp.24-25). However, we disagree with the committee's decision not to specify professions that ought to make up the specialist team (Evidence Review I p.23 lines 26-30), as we consider this will lead to people with ME/CFS undergoing multiple appointments with different healthcare professionals (HCPs), regardless of coordination of care by a named contact. It also risks issues being dealt with by therapists of the wrong specialism, risking mismanagement and harms to people with ME/CFS. There is the further concern that someone allocated, for example, a psychologist, as their point of contact, will avoid further use of the service even when they need help, because they do not see the relevance of psychology to their need. To remedy this risk of worsening for people with ME/CFS, we recommend the guideline specify a streamlined specialist team, led by a consultant of a suitable biomedical discipline with specialist knowledge of ME/CFS, who would confirm diagnosis,	The first recommendation in the multidisciplinary section states that this is a coordinated multidisciplinary approach and as such the title of this section has not been changed. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. The committee agree that the evidence base is limited and as outlined in the committee discussion they were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence. But they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). As you note certain skills are not necessarily restricted to a specific professional and this recognises this. The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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				order appropriate tests and referrals if needed and oversee care. Specialist nurses with up-to-date training consistent with this guideline would then fulfil the role of main point of contact for the person with ME/CFS and provide comprehensive support and care for most issues for which the person with ME/CFS may seek input. This would more closely mirror the NICE guideline for multiple sclerosis (CG186), in which a consultant of appropriate discipline (neurologist) and MS specialist nurses are specified to form part of the team. Rationale: The evidence for a multidisciplinary approach to care in ME/CFS is unacceptably low, with only two studies included on the basis they were the only evidence despite not comparing different multidisciplinary teams (MDTs) (Evidence Review I, p.9). Both were of low to very low-quality evidence (Evidence Review I, p.22 line 1). The quantitative evidence was stated to be limited and thus the cost-effectiveness of ME/CFS specialist MDTs uncertain (Evidence Review I, p.25, lines 26-27). One cost-utility analysis found multidisciplinary rehabilitation (physical therapist, occupational therapist, psychologist and social worker) not to be cost effective compared to CBT (ICER £106,000 per QALY gained. Evidence Review I, p.20). It is acknowledged that cost-effectiveness is *'likely to depend on the staff-mix in the team and the therapies offered.'* (Evidence Review I, p.25 lines 27-28.) In light of the dearth of effectiveness and cost-effectiveness data, it is therefore hard to understand the leap of logic made in the following statement: *'The exact cost effectiveness of a specialist team is uncertain, but the committee were convinced that their provision would be a good use of NHS resources, leading to faster access to appropriate care and substantially better patient outcomes for people with ME/CFS.'* (Evidence Review I, p.25 line 48 - p.26 lines 1-3.)	The committee agree that the evidence for the cost effectiveness of multidisciplinary teams is poor and therefore do not make any specification of which specialties make up such a team. In the committee's opinion, based on the wealth of evidence reviewed for this guideline, an effective and cost effective ME/CFS service must involve staff who have expertise in ME/CFS and the specific skills, as was outlined recommendation 1.10.1. Such a service might consist primarily of a suitably trained medical consultant and specialist nurse, as you suggest. However, there are other team models that might meet those requirements equally well. Continuity of care This section of the guideline includes a recommendation that people with ME/CFS have a named contact. This provides continuity of care to coordinate the care and support plan, help accessing services and support during periods of relapse. Home visits The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. *Service design* This guideline focused on clinical recommendations and the committee did not comment on the specific design delivery of services, which can be determined locally.

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				We believe the model of care we propose would by comparison be streamlined and cost-effective. A specialist ME/CFS nurse would be able to provide competent care spanning a significant number of the areas of expertise specified at 1.10.1 (also Evidence Review I, p.26, lines 11-20), and would therefore be able to provide post-diagnosis support and education on a wide range of issues, including energy management, Post Exertional Malaise (PEM) and prolonged deterioration (flares and relapses), symptom management (including medication review), dietary and mobility issues, and be able to provide informal support for emotional wellbeing (See Evidence Review G, p.325, lines 5-9 re importance of someone being available to talk to if help is needed as a form of safeguard). They can support the person with ME/CFS to learn the skills and strategies to self-manage effectively, and provide support if the person with ME/CFS overexerts themselves and experiences worsening (Re importance of these, see Evidence Review G, p.322, lines 33-35, 42-43). Nurses would be able to provide such support by phone, email or home visit and deal with multiple issues in one interaction. In contrast, therapists from various disciplines such as CBT, physiotherapy and occupational therapy, would be hampered by the narrowness of their field, and would be unable to fulfil such a role without exceeding the bounds of their expertise. The provision of care and support by a specialist nurse as main point of contact would therefore reduce risk of worsening to people with ME/CFS by virtue of multiple appointments with multiple HCPs and inappropriate management advice, and would be comparatively cost-effective. We agree with the statement in Evidence Review I that most people with ME/CFS will only require a few elements of the areas of expertise specified and only at specific points in time (p.26 line	

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				21). We think early, accurate diagnosis by a consultant with up-to-date knowledge of ME/CFS combined with specialist nurse post-diagnosis support will field most of these elements and reduce the extent and range of healthcare provision required downstream. Provision of care: Such provision would allow for continuity of care and for the specialist nurse to familiarise themselves with the individual circumstances of the person with ME/CFS, as recommended in NICE clinical guideline 'Patient experience in adult NHS services' (CG138). People with mild or moderate ME/CFS may prefer their GP to provide ongoing care or may choose to continue to consult the specialist nurse. People with severe to very severe ME/CFS, are likely to need to continue to be cared for by the specialist team, in conjunction with their GP. Where the person with ME/CFS is referred to a different specialism for investigation of symptoms, the consultant would explain the limitations and particular needs of the person with ME/CFS so that these can be accommodated. Access to specialist services will be difficult for many patients either geographically or because they are too sick to travel. Provision should be made for phone and online access, and home visits by the specialist nurse. In keeping with the Multiple Sclerosis (MS) guideline (CG186) and absence of reliable evidence for CBT to cure, treat or support to manage the symptoms of ME/CFS (Evidence Review G, pp.72-119, p. 318 line 23), we do not think the specialist team should be specified to include CBT therapists. Any qualitative	

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				evidence that some people find CBT helpful appears to be largely based on the non-specific skills of a good listener who has rapport with and believes the patient, and whom the patient feels they can contact for support if needed, not on the particular modality of psychological support. (Non-specific benefits of CBT noted in Evidence Review G, p.324 lines 41-43). Such elements of care can be provided by an empathic specialist nurse. For those needing further emotional support, access can be provided to a psychological therapist. We strongly recommend it be specified that specialist teams should not be led by a mental health specialist, psychiatrist, psychologist, or psychological therapist. We regard stating this in the guideline to be necessary as the draft guideline recommendations represent a significant departure from the 2007 NICE guideline (CG53), on which most current services are based. Their service model is no longer appropriate now that GET and directive CBT that is intended to treat ME/CFS are specifically excluded from the guideline.	
Science for ME (S4ME)	Guideline	022	021	Delete this line. There is no evidence that patients with ME/CFS have emotional needs as part of their core condition any more than those with other chronic disabling diseases have. Specifying this in the guideline seems to perpetuate the myth that people with ME/CFS are particularly emotionally susceptible, or need help with sexual relationships in a way that is not specified in, for example, the Multiple Sclerosis (MS) guideline.	Thank you for your comment. The committee disagree, emotional wellbeing is an important part of a holistic health approach. People with ME/CFS should have access to people with this expertise if required.
Science for ME (S4ME)	Guideline	023	007 - 010	We support the need for a named contact and think this should be specified as someone with a medical, not a therapy, specialism, likely best served by a specialist nurse, as is provided for other chronic disabling diseases.	Thank you for your comment. The committee discussed whether it was appropriate to name a specific nominated professional but concluded that the most appropriate professional may vary within and between across services and that this would part of local decision making.
Science for ME (S4ME)	Guideline	023	005 - 006	Providing they would not prefer a GP to oversee their care, we recommend that people with ME/CFS of all severity levels should remain under the overall management of a consultant, with the GP and/or specialist nurse providing services as required. Very	Thank you for your comment. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support

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				few GPs have the time or knowledge to provide helpful input either in daily management, or in dealing with severe cases. The specialist nurse is likely to have much more knowledge of ME/CFS than the GP, and would be accessible by phone, email or home visit and provide vital liaison with the consultant.	plan and supervision for the management of some symptoms. However the committee agreed that not everyone with ME/CFS would require or want the ongoing input from a specialist team and this is reflected in the following recommendation about the named contact being either in primary care or the ME/CFS specialist team. The named contact is the professional best placed to co-ordinate someone's care and this will be according to the person with ME/CFS circumstances. See evidence review I multidisciplinary care for the committee discussion.
Science for ME (S4ME)	Guideline	024	021 - 024	Should be deleted and replaced with an explanation of the concept of symptom-contingent pacing, whereby the person with ME/CFS controls their activity level to minimise Post Exertional Malaise (PEM) and the symptoms of ME/CFS. There is no evidence that increasing activity leads to improvement in people with ME/CFS. 'Progression' when symptoms are improved may still instigate PEM or prolonged deterioration (relapse). 'Pull back' is vague and does not convey the extent of reduction that may be needed. Replace with: • *'Utilises symptom-contingent pacing to avoid PEM, whereby the person adjusts activity levels based on how they feel;* • *does not have increasing activity as its objective, even in flexible increments;;* • *can be difficult due to symptom fluctuation and as not all energy demands are predictable;* • *requires that the person has requisite support, and has living and (if appropriate) work/education environments where the required actions such as limiting activity, pausing tasks and resting can occur.'*	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). .

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Science for ME (S4ME)	Guideline	024	018 - 020	It is not realistic to expect a healthcare professional to be on hand to recognise when a person with ME/CFS is approaching their limit. The aim of any professional input should be to equip the person (and family if necessary) with knowledge for self-management. Replace with : • *requires the person learn from experience to identify a level of activity that is normally safe, relationships between levels of activity and symptoms, and warning signs they should rest;* • *can include help from a healthcare professional to recognise relationships between levels of activity and symptoms, particularly for children and young people who may find it harder to judge their limits and can overreach them;*	Thank you for your comment. The committee agree and have recommended that energy management is a self-management strategy led by the person themselves with support from a healthcare professional in a ME/CFS specialist team.
Science for ME (S4ME)	Guideline	024	004 - 005	We agree with this statement and its inclusion in the guideline.	Thank you for your comment. *Cure or treatment* To note that after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Science for ME (S4ME)	Guideline	024	011 - 012	The person with ME/CFS will have the most insight as to how they are impacted by activity. There is no need to say of a self-management strategy that the person themselves leads it, and, after the person with ME/CFS has learned the principles, there may not be a need for the involvement of a health professional. Replace with:	Thank you for your comment. The committee agree that the person with ME/CFS is in charge of the aims of their care and this is clear in the principles of care section of the guideline. However the committee discussed that it is important that people with ME/CFS are supported a healthcare professional to recognise when they are approaching their limit (children and young people in particular may find it harder to

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				'is a self-management strategy for people with ME/CFS that involves: *a. limiting activity to minimise symptoms, primarily PEM;* *b. reserving capacity for activities that matter most to the person with ME/CFS.'*	judge their limits and can overreach them) as in their experience people often want to do more and risk PEM.
Science for ME (S4ME)	Guideline	024	014 - 015	Metaphors like 'energy envelope' may confuse readers and introduce untested terminology that will be unfamiliar to healthcare professionals (HCPs). It is better to convey in plain language that 'energy management' can help people to gauge how to avoid over-exerting themselves to reduce occurrence of PEM. We suggest use of the term 'symptom-contingent pacing' to convey in plain language that activity levels should be judged on current symptoms and the likely impact of activity on these with the object of avoiding PEM. This term can be clearly contrasted with potentially harmful forms of pacing, such as schedule-contingent or activity-contingent pacing. Including explanations of these terms in the guideline may go some way to address the issue raised by the Committee of the range of interpretations and lack of a standard definition for the term 'pacing' (Evidence Review G, p.322 lines 5-11). See https://www.physiosforme.com/pacing for information on symptom-contingent pacing. Replace with: '*[Energy management] does not involve undertaking the same amount of activity every day, as in order to avoid PEM, activity levels should be adjusted according to symptoms and the need for pre-emptive rest.'*	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits'. *Terms used in the guideline* After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
Science for ME (S4ME)	Guideline	024	007	We suggest substantial revision of subsection 1.11.2 to incorporate the following: '[Energy management]: *1. Is not curative and should not be expected to result in an*	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to make these edits to the recommendation:, • is not curative

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				increase in capacity for activity over time; *2. Is a self-management strategy for people with ME/CFS that involves:* *a. limiting activity to minimise symptoms, primarily PEM* *b. reserving capacity for activities that matter most to the person with ME/CFS;* *3. Takes into consideration the cumulative effects of all activity (both physical and cognitive) and the mitigating effects of rest;* *4. Recognises that each person has a different and fluctuating energy limit, and they are the best judge of their own limits (lines 16-17);* *5. does not involve undertaking the same amount of activity every day, as to avoid PEM activity levels should be adjusted according to symptoms and the need for pre-emptive rest;* *6. requires the person learn from experience to identify a level of activity that is normally safe, relationships between levels of activity and symptoms, and warning signs they should rest;* *7. can include help from a healthcare professional to recognise relationships between levels of activity and symptoms, particularly for children and young people who may find it harder to judge their limits and can overreach them;* *8. Utilises symptom-contingent pacing to avoid PEM, whereby the person adjusts activity levels based on how they feel;* *9. does not have increasing activity as its objective, even in flexible increments;* *10. can be difficult due to symptom fluctuation and as not all energy demands are predictable;* *11. requires that the person has requisite support, and has living and (if appropriate) work/education environments where the required actions such as limiting activity, pausing tasks and resting can occur.* *12. is not based on any hypothesis about the cause of ME/CFS,* as no cause of ME/CFS has been established.	• is a self-management strategy led by the person themselves with support from a healthcare professional in a ME/CFS specialist team • includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity • helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits • recognises that each person has a different and fluctuating energy limit and they are experts in judging their own limits • includes help from a healthcare professional to recognise when they are approaching their limit (children and young people in particular may find it harder to judge their limits and can overreach them) • uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse) • is a long-term approach − it can take weeks, months or sometimes even years to reach stabilisation or to increase activity. **The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context.**

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Science for ME (S4ME)	Guideline	024	013	Replace with: *'takes into consideration the cumulative affects of all activity (both physical and cognitive) and the mitigating effects of rest.'*	Thank you for your comment. This has been edited to.' includes all types of activity (cognitive, physical, emotional and social) and takes into account overall level of activity'.
Science for ME (S4ME)	Guideline	025	004 - 014	In its current form, 1.11.3 focuses on the healthcare professional (HCP) extracting information and delivering plans. Explicit mention of practical assistance on matters like helping the person to consider stopping or reducing work/school and helping them to implement any decisions they make is missing. These are things that will have significant impact on the person with ME/CFS' health and quality of life and should happen before any formal energy management planning. There is no point, for example, making an energy management plan for the situation of the person working full-time if, with some discussion, the person would have decided they needed to be working part-time. We suggest insertion of a new recommendation between 1.11.2 and 1.11.3 on information about energy management that should be discussed with the person with ME/CFS. Suggested wording and points for inclusion: '*Provide the person with ME/CFS with information from reliable sources about energy management (including 'symptom-contingent pacing')*. Discuss the following with them: *1. Their current activity and rest pattern and symptoms. This may be helped by the person keeping a symptom and activity diary in advance of the consultation;* *2. Planning for increased flexibility to allow increased rest and reduced activity. This may include stopping or reducing work/school or ensuring there are suitable places for scheduled rests;* *3. Communicating with friends and family re how best they can provide support;* *4. Finding ways to reduce daily activity whilst maintaining quality*	Thank you for your comment. The first and this recommendation emphasises that energy management is discussed with the person with ME/CFS. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The areas you mention are included within the topics included in overview. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.

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				of life, e.g., delegating tasks, ceasing low priority activities, utilising adaptations to reduce exertion (mobility aids, Blue Badge, working or schooling from home); *5. reducing time in high energy demanding environments such as places that are noisy/bright (or using aids such as noise cancelling headphones or dark glasses);* *6. Planning responses to Post Exertional Malaise (PEM) and longer deterioration;* *7. Information on peer support;* *8. Assistance for friends and family who may need to adapt to these changes.'*	
Science for ME (S4ME)	Guideline	025	004 - 014	Not all people with ME/CFS will want or need an energy management plan, and many people with ME/CFS would benefit more from advice from healthcare professionals (HCPs) that enables them to better cope with ME/CFS, reduce activity, access aids and get in touch with patient organisations, than from focus on assessments to create energy management plans. Energy management plans place additional restrictions on already constrained lives; creating an environment where they can be followed is an activity in itself. For people with mild and moderate ME/CFS, plans are highly likely to be abandoned for more pragmatic approaches (see Evidence Review G p.323 lines 8-10), possibly leaving people feeling that they have failed. Members of our forum found the ambitious daily schedule approach of GetSetJulie for example, patronising and unworkable. Energy management planning may be of more relevance to people with severe or very severe ME/CFS, who may require highly predictable routines to prevent worsening from unpredictable energy expenditure. We suggest insertion of a new recommendation between 1.11.2 and 1.11.3 recognising the agency of people with ME/CFS in deciding whether they want or need an energy management	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.

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				plan. Suggested wording and points for inclusion: 'Recognise that: - *many people with ME/CFS will not want, require or even benefit from an energy management plan and ongoing professional assistance with energy management, particularly if initial discussions about energy management are done well and good resources are provided;* - *some people with ME/CFS may not be able to decrease activity levels to a level that usually prevents PEM without additional practical support and care, or at all. In these cases, securing the support and care should take priority over completing an energy management plan;* - *the person with ME/CFS should be able to choose whether to have an energy management plan or not, or to stop or restart an energy management planning process.'*	
Science for ME (S4ME)	Guideline	025	004 - 014	We suggest addition of a bullet point for the sensory impact of the person with ME/CFS' home and (if relevant) work/school environments, including light and sound exposure. Suggested wording: '*sensory sensitivities including light and sound exposure at home and work or school if relevant*'	Thank you for your comment. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The area you mention is included within the topics included in overview. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.
Science for ME (S4ME)	Guideline	025	004 - 014	We suggest addition of a bullet point that the plan should cover responses to a deterioration of symptoms. Suggested wording: *'ability to recognise and appropriately manage PEM and periods of longer deterioration'*	Thank you for your comment. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The beginning of the recommendation also

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					includes, discuss, 'along with anything else that is important to the person'. Recommendation 1.11.2 includes to discuss the principles of energy management and this includes that it helps people learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits and in recommendation 1.11.6 it now includes , 'advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'
Science for ME (S4ME)	Guideline	025	015 - 022	Recommendation 1.11.4 is too oriented to forward planning of activities, and makes no mention of taking notice of symptoms. It is based on the assumption the patient knows their 'energy envelope', a term we have advised against using, and something many people will find difficult to estimate. The words 'as the first step' should be deleted. Replace section 1.11.4 with: *If the person wishes, help them make an energy management plan. This notes how they will manage periods of rest, activity and pre-emptive rest. Ensure that any plan is flexible so the patient can be guided by their symptoms to take sufficient rest breaks during activities, and to reduce activity and rest more if symptoms worsen.*	Thank you for your comment. This recommendation is about the strategies in an energy management plan the following recommendations address recognising and managing flare-ups. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This applies to the energy management plan.
Science for ME (S4ME)	Guideline	025	004 - 006	The words 'goals' and 'expectations' though qualified with 'realistic' create an expectation goals will be set and worked towards. This may cause harm either by assuming the person with ME/CFS should increase activity to achieve a goal or by creating a sense of failure if they cannot. Further, some people may not want or need a management plan. There is no reliable evidence for 'benefits in setting of goals'. In Evidence Review G	Thank you for your comment. The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the

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				(p.336, lines 23-35), it is acknowledged that rigid or unrealistic goals can lead to deterioration and feelings of pressure and blame. A goal that is unrealistic or rigid to a person with ME/CFS may seem achievable to a healthcare professional (HCP), leading to conflict and feelings of pressure and blame. Suggested replacement wording: *'If the person with ME/CFS would like an energy management plan, discuss and record the person's:*'	guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. The beginning of this section is clear that this is a self-management strategy led by the person themselves with support from a healthcare professional in a ME/CFS specialist team. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. In the section of flare ups and relapses now linked to in this section the committee have added a recommendation raising awareness that flare-ups and relapses can happen in ME/CFS even if the person's symptoms are well managed.
Science for ME (S4ME)	Guideline	025	027 - 029	To take into account not all people with ME/CFS will want or need to track activity and symptoms, we suggest the alternative wording: '*Some people with ME/CFS may find it useful to track activity and symptoms to understand patterns, especially early in the illness. Tools such as activity trackers, heart rate monitors, apps and diaries may help with this.*' See Evidence Review G (p.336 lines 36-42), where potential harms of increased burden of tracking is acknowledged.	Thank you for your comment. In the rationale section the committee recognise there was a lack of effectiveness evidence on tools to support people to self-monitor activity management. The committee decided to recommend that activity recording should be as easy as possible, and people should take advantage of tools they are already using and gave examples of these. The committee also decided to make a recommendation for research on self-monitoring management strategies to help determine which techniques are effective.

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					The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Science for ME (S4ME)	Guideline	025	001 - 002	Should be deleted. There is no evidence that energy management results in an increase in activity levels over time, or even stabilises the illness.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse).
Science for ME (S4ME)	Guideline	025	023 - 024	Replace with: *'During periodic care reviews, the person with ME/CFS should be asked about their energy management and the frequency of PEM.*'	Thank you for your comment. This recommendation addresses the strategies in an energy management and the following recommendation is about reviewing the energy management plan. It is within the review questions about energy management and frequency of PEM would take place.
Science for ME (S4ME)	Guideline	025	025 - 026	This clause should include that reducing activity should be advised if Post Exertional Malaise (PEM) is present and there should be recognition of the effect on function and support needs of PEM or prolonged deterioration (relapse). Most people with ME/CFS have symptoms most of the time and regularly have fluctuations in daily energy levels. The words	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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				'*reduce their activity if increasing it triggers symptoms*' implies that people with ME/CFS should be increasing activity. Replace lines 25-26 with: *'Advise people with ME/CFS to reduce their activity if their symptoms worsen or PEM is present. Discuss what support they may need to reduce their activity.* *If they are feeling better, they may naturally want to do more, but all increasing should be done gradually to avoid PEM or deterioration. Increased activity may appear to be sustainable for a few days or weeks, but may lead to prolonged deterioration (relapse). Any increase should be small, and not further increased unless activity at that new level can be sustained along with the improvement in symptoms maintained for weeks.'*	
Science for ME (S4ME)	Guideline	025	003	If such a statement is included, it should be more encompassing since there are a number of unevidenced and harmful hypotheses on cause that may be invoked in connection with energy management. Suggested wording: '*[Energy management] is not based on any hypothesis about the cause of ME/CFS, as no cause of ME/CFS has been established.*'	Thank you for your comment. The committee deleted the bullet point on deconditioning noting that this recommendation was about providing advice to people with ME/CFS about the approaches to implement energy management and this point was not useful in this context
Science for ME (S4ME)	Guideline	025	009	Add 'and whether the person has or needs help.'	Thank you for your comment. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.
Science for ME (S4ME)	Guideline	026	001 - 007	Recommendation 1.11.8 currently assumes that people with ME/CFS must have professional assistance in the circumstances specified. The guideline should make clear that referrals must always be contingent on informed consent based on the person with ME/CFS genuinely wanting the assistance.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about

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				Replace with: *'If a person with ME/CFS wants assistance:* - *with energy management, including support developing an energy management plan; or* - *to access and use energy-saving tools and mobility aids.* *refer them to a physiotherapist, occupational therapist, or specialist nurse who has up-to-date training in ME/CFS management that is in accordance with this guideline.'* If a person has had 'r*educed physical activity or mobility levels for a long time*' but is managing their illness well, we do not see what is to be achieved by referral. People with ME/CFS who start to improve are likely to be able to successfully increase activity naturally on their own. Referral may be of use to people who have been largely immobile for a long period, but a clause addressing this should be much more carefully worded and consider limitations of people with severe or very severe ME/CFS, to whom it will mostly apply.	their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service.
Science for ME (S4ME)	Guideline	026	017 - 022	Include dental health in 1.11.11. Dental consultations present problems of travel, being upright for wait time and coping with examination for people with ME/CFS.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added. Dental health has been added into recommendation 1.10.1 to highlight its importance.
Science for ME (S4ME)	Guideline	026	017 - 022	We suggest inclusion of sensible examples of appropriate physical maintenance. Eg., '*Muscle flexibility e.g. gentle stretches in bed*.'	Thank you for your comment. After considering the range of stakeholder comments the committee agreed to remove the examples in the rationale recognising that approaches will be individual and in the context of the priorities and abilities that people may have. Based on this they agreed not to include examples in the recommendations.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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Science for ME (S4ME)	Guideline	026	012 - 015	This clause should be revised. The words 'when agreeing' are not appropriate, as they suggest compromise where parties differ, leading to the person with ME/CFS 'agreeing' to do more than they are able without worsening. Changes in activity for mild and moderate cases may also need to be small and slow or may not be possible; the clause implies this is only the case for severe and very severe.	Thank you for your comment. The additional recommendations on people with severe to very severe ME/CFS are to ensure that additional caution is taken. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Science for ME (S4ME)	Guideline	026	009 - 011	Subject to informed consent and genuinely wanting referral, any person with ME/CFS, regardless of severity level, who would like assistance with energy management or creating an energy management plan should be referred to a specialist physiotherapist, occupational therapist or specialist nurse with up-to-date training in ME/CFS consistent with this guideline. An ill-informed healthcare professional (HCP) can do much greater harm than the absence of a formal energy management plan. A person with ME/CFS may find their activity affected by other symptoms than fatigability, such as orthostatic intolerance, pain and sleep problems which need to be managed in conjunction with energy management. A specialist nurse would be best qualified to see the full picture. If retained, 1.11.9 should link to 1.8 Access to care.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, F,G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is

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					important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service. The committee agreed that for people with ME/CFS it was important that the healthcare professionals with the appropriate clinical background and training supported any physical activity plans, here physiotherapist or occupational therapists.
Science for ME (S4ME)	Guideline	026	017 - 018	After the first sentence, we suggest adding: *'Any proposal for physical maintenance needs to be based on a realistic assessment of the person's ability to sustain the action. The possibility of causing PEM, consequent reduction in function and lowered PEM threshold, alongside displacement of essential activities should be weighed carefully against likely benefits of any physical maintenance.'*	Thank you for your comment. 'strategies need to be carried out in small amounts and spread out throughout the day' has been added to the first recommendation in this section to clarify that any strategies implemented are in the context of the priorities and symptoms that people may have. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management

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					section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.
Science for ME (S4ME)	Guideline	026	015	Include a recommendation after 1.11.10 that includes the following: *'Energy management planning for people with severe or very severe ME/CFS requires a high level of specialist knowledge. Balancing a need for social connection and quality of life with the fact that even a short time on an electronic device or a small amount of talking can have a significant impact on symptoms is difficult. Health professionals who have not done energy planning for people with ME/CFS who are severely or very severely affected must first get advice from others who have.* *'Recognise that deterioration in functioning can result in the person needing a very high level of care. The energy management plan should set out what will be done when this happens, including how the extra support will be provided.'*	Thank you for your comment. The committee have recommended that people with severe or very severe ME/CFS should be referred to a specialist ME/CFS physiotherapy or occupational therapy service for support on developing energy management plans. The care and support plan and the energy management plans include guidance on managing flares and relapses. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason you suggestion has not been added.
Science for ME (S4ME)	Guideline	026	016	We think the subsection, 'Physical maintenance' is a helpful, practical subsection that can make a difference to the well-being of people with ME/CFS and their carers.	Thank you for your comment.
Science for ME (S4ME)	Guideline	027	021 - 023	This clause needs clarifying. It is not clear if supervised unstructured or unsupervised structured exercise is acceptable and these terms are not defined. Suggested edit: '*Do not advise people with ME/CFS to undertake general exercise, such as telling them to go to the gym or to exercise more, as this may worsen their symptoms*.'	Thank you for your comment. After considering the stakeholder comments this has been edited to, 'do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.'
Science for ME (S4ME)	Guideline	027	020	Comment on the subsection 'Physical activity': We are pleased the committee recognises the high risk of bias presented by open label trials with subjective outcome measures,	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical

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				the impact of this on interpreting evidence, and that there is no good quality evidence that exercise or activity programmes are effective treatments or cures for ME/CFS (Evidence Review G, pp. 137-165, 334-335; Draft guideline: Rationale and impact, p.63 lines 7-8). However, on the same basis, there should be no recommendation to offer physical activity programmes in this guideline. Therefore, the content of the subsection on physical activity should be deleted and replaced with a clear statement outlining types of activity and exercise programmes that should not be offered to people with ME/CFS. Rationale: There is no reliable evidence that physical activity programmes are effective in treating or managing ME/CFS, or increasing function or tolerance to activity in people with ME/CFS (which may be viewed as treating). Evidence quality for all GET and other exercise intervention studies was judged to be low or very low, with inconsistency of findings across outcome measures (Evidence Review G pp.137-165, 334-335). The recommendations on considering physical activity programmes for people with ME/CFS (1.11.17 - 1.11.20) therefore introduce confusion to the guideline as to which types of activity programme are acceptable and which are not. The recommendation not to offer any therapy based on physical activity or exercise as a treatment or cure for ME/CFS is thus weakened. Existing GET programmes that are nominally compliant (e.g. by allowing increase by flexible increments) will remain in place under the new guise of 'optional physical activity programmes', and continue to do harm to people with ME/CFS. It has been	activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about

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				suggested by GET proponents that the poor objective outcomes and high drop out rates reported for ME/CFS specialist clinics, and the lack of support for GET from people with ME/CFS is due to an implementation problem. However, even under clinical trial conditions with delivery by well trained experts, there has been no objective evidence of benefit from any exercise or activity program. We are pleased to see the guidance not to offer any therapy based on physical activity or exercise as a treatment or cure for ME/CFS (p.28 lines 1-2) and some of the specific guidance not to offer certain types of physical activity or exercise programmes and therapies in 1.11.16. However, the section on 'Physical activity' does not go far enough to protect people with ME/CFS from harmful programmes. There is no justification for offering any sort of activity programme to people able to mobilise without aids. 'Programmes', however slow and gentle, are by their nature timetabled and structured, and often done in a group setting, which can encourage people to push through to keep up with the group. It is inappropriate to offer activity programmes to people if they 'would like' them as this offers a false version of patient choice, implying by the existence of such a programme that it will improve the person's health, or the NHS would not be offering it. People with ME/CFS long to be able to do more, and find it difficult to manage cutting back their activities sufficiently to avoid PEM. Any suggestion that an activity programme might be helpful if they 'would like' it, is not supported by evidence. We propose the content of the 'Physical activity' section be deleted and replaced with the following:	experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. *Treatment or cure* To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to

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				1. People with ME/CFS need advice and support to rest and avoid over-exerting to minimise PEM. If a person feels they are able to increase activity, they should be advised to proceed cautiously, particularly on good days when they may think they can do more without resulting PEM. If requested, referral to a specialist physiotherapist with up-to-date training in ME/CFS consistent with this guideline should be provided to those with problems mobilising without aids who need specialist advice. *2. If able to increase, people with ME/CFS, particularly if already ambulant, will generally do this naturally without input from a* healthcare professional (*HCP).* *3. 'Activity' and 'physical activity' are defined in the guideline and HCPs should recognise that an increase of any type of activity, however seemingly trivial, may cause worsening for people with severe or very severe ME/CFS.* *4. Do not advise people with ME/CFS to undertake general exercise, such as going to the gym or exercising more, because this may worsen their symptoms.* *5. Therapy based on physical activity or exercise is not a treatment or cure for ME/CFS and should not be offered as such.* *6. There is no reliable evidence that physical activity programmes are effective in managing ME/CFS or its symptoms, or increasing function or tolerance to activity. They should not be offered as such.* *7. Offering activity programmes with the objective of managing ME/CFS or its symptoms, or increasing function or tolerance to activity, can be regarded as offering them to treat ME/CFS. Any therapy based on physical activity or exercise as a treatment or cure for ME/CFS should not be offered* (Rationale and impact, p.63 lines 7-8). *8. Do not offer the following to people with ME/CFS:* *a. generalised physical activity or exercise programmes. This includes programmes developed for healthy people or people with other illnesses;* *b. any programme that has increasing activity or exercise as its*	avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS.

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				objective, regardless of whether this is by fixed or flexible increments, for example graded exercise therapy; *c. any activity or exercise programme based on a hypothesis of the cause of ME/CFS, as this is not yet known. This includes activity or exercise programmes based on deconditioning, central sensitisation, or fear avoidance, and ones that aim to desensitise people with ME/CFS to exertion or triggers (eg., light, sound) through exposure.* *d. therapies derived from osteopathy, life coaching and neurolinguistic programming (for example the Lightning Process).* We are pleased that some of the above is addressed at 1.11.15 and 1.11.16. However, we do not feel the guideline adequately protects patients from harm in its current form.	
Science for ME (S4ME)	Guideline	027	020	We provide comments on each recommendation in support of our suggestion to replace the current 'Physical activity' section as outlined above. These comments should also be considered as stand alone feedback.	Thank you for your comment.
Science for ME (S4ME)	Guideline	028	001 - 011	Include an additional recommendation after 1.11.16: '*There is no reliable evidence that activity programmes are effective in managing ME/CFS or its symptoms or increasing function or tolerance to activity. Therefore they should not be offered as such.*'	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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					*See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Science for ME (S4ME)	Guideline	028	012 - 015	Should be deleted and replaced with: '*People with ME/CFS will typically naturally increase physical activity if there is an increase in capacity. Advise taking any increases in activity slowly and to cut back and rest more if symptoms increase. Refer to a specialist physiotherapist with up-to-date ME/CFS training consistent with this guideline if requested.'* Rationale: The recommendation for physical activity programmes in this section gives mixed messages about the acceptability of activity programmes and will lead to inappropriate programmes continuing in place with resultant harms to people with ME/CFS. The words '*incorporate physical activity into the management of their ME/CFS'* suggests such programmes may be used to manage ME/CFS. There is no reliable evidence for this. Evidence quality for all GET and other exercise intervention studies were judged to be of low or very low evidence quality, with inconsistency of findings across outcome measures (Evidence Review G pp.137-165, 334-335). If a condition is successfully managed by a programme, then it is treated by it; the guideline states that therapy based on physical activity should not be offered as a treatment for ME/CFS (1.11.16; Rationale and impact, p.63 lines 7-8). The words '*ready to progress their physical activity*' imply	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and

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				patients are failing in condition management in some sense if not able to increase activity. Use of the word 'or' in line 14 suggests that people who would like to do some more physical activity should be offered it, regardless of whether they are able to progress their activity beyond their current activities of daily living or not.	Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise

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					or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. *Ready to progress* After considering stakeholder comments this bullet point has been edited to,' feel ready'.
Science for ME (S4ME)	Guideline	028	019 - 022	Self report is not sufficient basis for a recommendation, and is often contradicted in trials of adequate methodology (e.g. where sufficient blinding and/or objective outcome measures are employed). There is no reliable evidence of benefits of a physical activity programme, yet this recommendation claims benefit without specifying what it is. A therapy that leads to benefits must be regarded as a treatment; the guideline specifies therapy based on physical activity or exercise should not be offered as a treatment or cure for ME/CFS (1.11.16; Rationale and impact, p.63 lines 7-8). Many have reported long-term and significant worsening after an activity or exercise programme; this clause does not adequately convey risk. Statements like this should not be in an evidence-based guideline.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise

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					interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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Science for ME (S4ME)	Guideline	028	003 - 005	Good. Should be retained.	Thank you for your comment.
Science for ME (S4ME)	Guideline	028	016 - 018	If retained, should specify programmes offered should be consistent with this guideline. Physiotherapists and occupational therapists delivering such programmes should have up-to-date ME/CFS training consistent with this guideline.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Science for ME (S4ME)	Guideline	028	001 - 002	Suggest replace with '*Any therapy based on physical activity or exercise as it is not a treatment or cure for ME/CFS and should not be offered as such.*' (Rationale and impact, p.63 lines 7-8).	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
Science for ME (S4ME)	Guideline	028	006 - 007	Suggest replace with: '*any programme that has increasing activity or exercise as its objective, regardless of whether this is by fixed or flexible increments, for example graded exercise therapy.*' By specifying that programmes based on fixed incremental increases should not be offered, any programme based on flexible increases would remain acceptable under the guideline. E.g. Programmes with scheduled increases except when PEM is present may be viewed as incorporating flexible increments and therefore guideline compliant, yet may do significant harm. There is no standard definition of GET (Evidence Review G, p.335 lines 8-10), and therefore no requirement that increases in GET programmes must be by fixed increments. It can be seen from Evidence Review H that, in fact, studies of GET included in the evidence review did include flexible increments. It is therefore clear that the portrayal of programmes involving fixed increments	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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				as poorly evidenced and potentially harmful and programmes involving flexible increments as of potential benefit is a false distinction; studies of GET programmes have been assessed as low or very low quality evidence regardless of whether they involve fixed or flexible increments, with inconsistency of findings across outcome measures (Evidence Review G pp.137-165, 334-335). We provide excerpts from study summaries in Evidence Review H, illustrating increasing by non-fixed increments: Broadbent (2016), pp.34-35: *'Exercise sessions were progressed by increasing the duration of the session only as tolerated for each participant. The workload was not increased until participants had achieved three consecutive exercise sessions of 30 min in total with no increase in symptoms, and the increase was 10% of the current workload. If participants reported any increase in fatigue or other symptoms during post-exercise, the exercise intensity was reduced until participants felt able to manage progression.'* Clark (2017), pp.92-93: *'If symptoms increased after an incremental change in activity, participants were advised to maintain activity at the same level until symptoms had settled, before considering another incremental increase.'* Wallman (2004), pp.230-231: *'Subjects were instructed to exercise every second day unless they had a relapse. If this occurred or if symptoms became worse, the next exercise session was shortened or cancelled and subsequent sessions were reduced to a length that subjects felt was manageable (pacing)'* Descriptions of other GET study interventions included in the	*See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). GET The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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				evidence review also indicated that increasing was not by fixed increment (Fulcher, 1997; Wearden, 1998; White, 2011). Further, Evidence Review G acknowledges the heterogeneity of interventions described in GET studies (p.335, lines 9-10). Therefore, it is not sufficient to recommend that 'any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy' should not be offered to people with ME/CFS. To accurately reflect the evidence and adequately protect people with ME/CFS from harms, lines 6-7 should recommend that all programmes that have increasing activity or exercise as their objective, regardless of whether this is by fixed or flexible increments, should not be offered to people with ME/CFS. This includes but is not limited to GET.	
Science for ME (S4ME)	Guideline	028	008 - 009	Delete 'structured'. Suggested edit: '*any activity or exercise programme based on a hypothesis of the cause of ME/CFS, as this is not yet known. This includes activity or exercise programmes based on deconditioning, central sensitisation, or fear avoidance, and ones that aim to desensitise people with ME/CFS to exertion or triggers (eg., light, sound) through exposure.*'	Thank you for your comment. After considering the stakeholder comments structured has been deleted. The point here is about the programmes based on the deconditioning theories and for that reason your suggestions have not been added.
Science for ME (S4ME)	Guideline	028	010 - 011	Good. Should be retained.	Thank you for your comment.
Science for ME (S4ME)	Guideline	028	025 - 026	We do not support the concept of a 'baseline' in ME/CFS, as this inaccurately implies a level of activity that does not cause PEM from which the person with ME/CFS can increase. 'PEM threshold' may be a more appropriate term. But such concepts translate less well to real life; many people with ME/CFS have little option but to routinely exceed their limits due to personal circumstances and obligations, and many with ME/CFS have no spare capacity to increase without inducing PEM. See Evidence Review G, p.333 lines 20-21 where (in reference to GET programmes) it is stated qualitative evidence showed '*baseline levels were not experienced as sustainable*' by people with ME/CFS.	Thank you for your comment. The committee agree the terminology is varied to describe someone's energy threshold. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. This is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly.

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Science for ME (S4ME)	Guideline	028	023	Recommendation 1.11.20 describes a form of graded exercise therapy and has no place in the guideline. It illustrates why it is not possible to recommend activity programmes without inadvertently sanctioning harmful activity programmes. The guidance to start by reducing activity and to '*use flexible increments for people who want to focus on improving their physical activities while remaining within their energy envelope*' is not sufficient to distinguish this from harmful activity programmes for which there is no reliable evidence of effectiveness, including GET. There is no standard definition of GET (Evidence Review G, p.335 lines 8-10), and therefore no requirement that increases in GET programmes must be by fixed increments. It can be seen from Evidence Review H that, in fact, studies of GET included in the evidence review did include flexible increments (Broadbent, 2016; Clark, 2017; Fulcher, 1997; Wallman, 2004; Wearden, 1998; White, 2011). It is therefore evident that the portrayal of programmes involving fixed increments as poorly evidenced and potentially harmful and programmes involving flexible increments as potentially helpful is a false distinction; studies of GET programmes have been assessed as low or very low quality evidence regardless of whether they involve fixed or flexible increments, with inconsistency of findings across outcome measures (Evidence Review G pp.137-165, 334-335). Therefore, it is not sufficient to recommend that '*any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy*' should not be offered to people with ME/CFS. To accurately reflect the evidence and adequately protect people with ME/CFS from harms, physical activity programmes should not be recommended in this guideline, irrespective of whether they involve increasing by fixed or flexible increments.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the

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				1.11.20 is overly prescriptive and may result in unworkably regimented routines, with worsening of or no reduction in symptoms and reduced quality of life. It appears to use the concepts of a 'baseline' and 'energy envelope' interchangeably and creates the expectation that physical activity can be successfully increased in flexible increments.	reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.

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					1.11.20 The committee note this is a collaborative personalised plan and the detail of the plan is individual to the person.
Science for ME (S4ME)	Guideline	029	008 - 013	We do not generally see the relevance of accessing specialist ME/CFS physiotherapy services during Post Exertional Malaise (PEM) or prolonged deterioration (relapse), when rest and reduction of activity should be prioritised. We suggest lines 8-13 be replaced with: '*reducing activity and increasing rest for as long as needed until symptoms improve, and being aware that after PEM or a longer deterioration, they may not be able to return to the previous level of activity. Access may be provided to a physiotherapist with up-to-date training consistent with this guideline for advice on physical maintenance if appropriate.'*	Thank you for your comment. The previous recommendation includes the importance of including how to recognise a flare-up or relapse early and outlining how to manage it. This recommendation includes access to a review and support and this is important for people who wish to access this support.
Science for ME (S4ME)	Guideline	029	018 - 022	Add a bullet point to 1.11.23: '*Where hypersomnia is present, do not restrict sleep*.' There is no reliable evidence that sleep restriction leads to a reduction of ME/CFS symptoms, and some patients and their carers report that it can cause harm. Unrefreshing sleep is one of the required symptoms for suspecting ME/CFS (p.8, Box 1). It is not something that can be resolved by standard sleep hygiene recommendations.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Science for ME (S4ME)	Guideline	029	018 - 022	Add a bullet point to 1.11.23: '*Sleep during the day may be helpful; the person with ME/CFS should find what works best for them*'.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored

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					to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Science for ME (S4ME)	Guideline	029	018 - 022	Add an additional bullet point to 1.11.23: '*that people with severe or very severe ME/CFS may need to spend extended periods or all of their time lying in a dark, completely quiet room with little or no stimulation in order to avoid worsening*.'	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Science for ME (S4ME)	Guideline	029	014 - 016	Add that they may need to adapt to a new lowered level of physical activity in the long-term.	Thank you for your comment. The collaborative personalised programme includes recognising a flare-up or relapse early and outlining how to manage it, as part of this any strategies would be individual and agreed with the person with ME/CFS
Science for ME (S4ME)	Guideline	029	001 - 002	Assumes that people with ME/CFS are not using all of their 'energy envelope' and so there is unused capacity that can be devoted to physical exercise. This is not true; people with ME/CFS struggle to restrict their activity to a safe level. Also assumes that 'energy envelope' capacity (capacity for activity without inducing Post Exertional Malaise (PEM)) will be increased once a physical activity programme is embarked on, otherwise it would not be possible to continue increasing whilst remaining inside the energy envelope. There is no reliable evidence that physical activity programmes lead to such an increase in capacity and no reason to think that such programmes will not lead to harms.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and

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					specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2).
Science for ME (S4ME)	Guideline	029	006 - 007	'Agree with' should be replaced with 'Discuss with'. The current wording may lead to the person with ME/CFS having to negotiate adjustments to physical activity with a healthcare professional (HCP) and compromise if views on activity levels differ.	Thank you for your comment. This is part of the personalised physical activity or exercise programme and discussion is fundamental in agreeing this.
Science for ME (S4ME)	Guideline	029	012 - 013	We do not support the concept of a 'baseline' in ME/CFS, as this inaccurately implies a level of activity that does not cause Post Exertional Malaise (PEM) from which the person with ME/CFS can increase. 'PEM threshold' may be a more appropriate term. But such concepts translate less well to real life; many people with ME/CFS have little option but to routinely exceed their limits due to personal circumstances and obligations, and many with ME/CFS have no spare capacity to increase without inducing PEM. See Evidence Review G, p.333 lines 20-21 where (in reference to GET programmes) it is stated qualitative evidence showed '*baseline levels were not experienced as sustainable*' by people with ME/CFS.	Thank you for your comment. The committee agree there is variation in how the concept of a baseline is describe in the ME/CFS community. It is used here to describe an appropriate level of physical activity discussed and agreed with the person with ME/CFS.

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Science for ME (S4ME)	Guideline	029	021 - 022	It is not appropriate for healthcare professionals (HCPs) to advise people with ME/CFS 'how often and for how long' rest periods should be. This should be determined on an ongoing basis by the person with ME/CFS. delete: '*including how often and for how long, as appropriate for each person*'	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Science for ME (S4ME)	Guideline	029	017	CBT should not be offered to support people to manage sleep issues in ME/CFS, as the evidence review found no reliable evidence of benefit of CBT for sleep quality, and quality of evidence for all outcomes across all CBT clinical studies included in the evidence review was found to be low or very low (Evidence Review G, p.323-324, 72-119).	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
Science for ME (S4ME)	Guideline	029	019	We are pleased to see that rest is recognised as key in managing ME/CFS. Add 'important', i.e., '*on the important role of rest in ME/CFS*'.	Thank you for your comment. In the rationale section the committee recognise the understanding the role of rest and how to introduce rest periods was important in successful energy management. As this

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					included here your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	030	007 - 012	After 1.11.26, add a recommendation: '*Any clinician treating a person with ME/CFS for orthostatic intolerance should have up-to-date ME/CFS training consistent with this guideline and therefore understand that exercise may worsen the symptoms of ME/CFS, including orthostatic intolerance.*'	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. In addition the managing co-existing conditions of section of the guideline also recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable for this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	030	013 - 016	Include that CBT should not be offered to support people to manage pain in ME/CFS, as there is no reliable evidence this leads to improvement. The evidence review showed no finding of benefit (versus usual care) and inconsistency of findings (versus other interventions) for pain outcomes, and quality of evidence for all outcomes across all CBT clinical studies included in the evidence review was found to be low or very low (Evidence Review G, pp. 72-119, 323-324).	Thank you for your comment. The managing co-existing conditions of section of the guideline recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
Science for ME (S4ME)	Guideline	030	013 - 016	Recommendation 1.11.27 should include more guidance on treating pain in ME/CFS, including '*pain on touch, myalgia,*	Thank you for your comment.

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				headaches, eye pain, abdominal pain or joint pain without acute redness, swelling or effusion'. These types of pain are described as symptoms that may be associated with ME/CFS at 1.2.4 (p.9, lines 15-16) of this draft guideline.	Pain relief was included as an intervention in the protocol for pharmacological interventions. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee agree that people with ME/CFS report many different types of pain. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Science for ME (S4ME)	Guideline	030	013 - 016	Add: '*Some people with ME/CFS find that over the counter pain medication may reduce their pain levels. Due to restricted mobility and access to shops, over the counter pain medication should be available by repeat prescription in packs larger than those available without prescription, subject to regular review and clear advice on dosing, side effects and risks of long-term use.*'	Thank you for your comment. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications or access to medications. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS. In the medicines for symptom management section of the guideline the committee recommend that people with ME/CFS have a medication review in line with the NICE guidelines on medicines adherence and medicines optimisation.
Science for ME (S4ME)	Guideline	030	013 - 016	Many people with ME/CFS have chronic pain and are often unable to engage in activities that could distract from the pain. This makes pain relief particularly important. Opioid pain relief is important for quality of life for some people with ME/CFS; access to this needs to be protected unless satisfactory alternatives can	Thank you for your comment. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee did

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				be provided. The NICE guideline on neuropathic pain in adults only refers to Tramadol in rare acute cases.	provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Science for ME (S4ME)	Guideline	030	013 - 016	Add: '*New or worsening pain symptoms should be appropriately investigated and not assumed to be caused by ME/CFS*.'	Thank you for your comment. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
Science for ME (S4ME)	Guideline	030	013 - 016	Include that if pain has been appropriately investigated, and cannot be managed in primary care, it is possible that people with ME/CFS will be referred on to a pain management clinic. It is essential that all clinicians involved have up-to-date ME/CFS training in accordance with this guideline. Some approaches to pain management, particularly those involving exercise programmes for management of pain, can be harmful to people with ME/CFS.	Thank you for your comment. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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Science for ME (S4ME)	Guideline	030	013 - 016	We note the recent confirmation by Dr Paul Chrisp of NICE that the draft NICE guideline on chronic pain does not and will not apply to people with ME/CFS. https://meassociation.org.uk/2020/0...-get-covid-19-and-new-guideline-chronic-pain/. This is important as the chronic pain guideline, with its focus on exercise, psychological therapies and alternative medicine, and withdrawal of pain relief drugs, is completely inappropriate for people with ME/CFS. Add: '*the NICE guideline on chronic pain does not apply to people with ME/CFS*.'	Thank you for your comment. The committee agree it is important that clinicians caring for people with ME/CFS are aware that when referring to other guidelines for the management of co-existing conditions they should be used with caution and some advice may be inappropriate. This is highlighted in the section on managing co-existing conditions in the guideline. It is unnecessary to add that the NICE guideline on chronic pain does not apply to people with ME/CFS, the absence of a reference implies this.
Science for ME (S4ME)	Guideline	030	001 - 002	Delete. This recommendation could be used to promote 'techniques' that have no more evidence to support them as being beneficial for rest or for ME/CFS symptoms than common sense approaches to achieving rest.	Thank you for your comment. As you note no evidence was identified to support recommending specific relaxation techniques for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any specific techniques but the committee recognised that some people find using relaxation helpful.
Science for ME (S4ME)	Guideline	030	002	Add a recommendation after 1.11.23 clarifying guidance for GPs on prescribing medication to help with sleep if a person with ME/CFS needs it.	Thank you for your comment and information. Although sleep medication was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any specific recommendations for medicines or prescribing. The committee have provided general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
Science for ME (S4ME)	Guideline	030	006	add: '*or hypertension*' after hypotension, as some people experience orthostatic hypertension and treatment for this is different.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added, after considering stakeholder comments POTS is the only example included..

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Science for ME (S4ME)	Guideline	030	006	After 1.11.24 insert a recommendation: '*Be aware that* in *those with severe and very severe ME*/CFS, *orthostatic intolerance may be very severe, and result in the person not being able to sit up for more than a few seconds or minutes, or at all.*'	**Thank you for your comment.** An additional sentence noting that people with severe orthostatic intolerance many find they are unable to sit up for any period of time has been added to the definition.
Science for ME (S4ME)	Guideline	031	001 - 004	Add: '*Prescribe medication for nausea if needed*.'	Thank you for your comment. In the absence of any evidence on dietary strategies or treatments for nausea the committee made a consensus recommendation with general advice (now in the dietary management section) and expanded on this in the committee discussion in Evidence review G- Non-pharmacological management.
Science for ME (S4ME)	Guideline	031	001 - 004	Add: '*New or worsening nausea symptoms should be investigated, rather than assumed to be part of ME/CFS*.'	Thank you for your comment. The committee agree that any symptoms should be investigated to rule out other diagnoses or coexisting conditions and if there is any uncertainty in interpreting signs or symptoms then advice should be sought from an appropriate specialist.
Science for ME (S4ME)	Guideline	031	014	add an additional bullet point regarding approaches to drug treatment of symptoms: • '*trialling different drugs one at a time*'	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
Science for ME (S4ME)	Guideline	032	007	After 1.11.34, add: '*Some people with ME/CFS, particularly with severe or very severe presentation, can develop difficulty eating due to gastrointestinal issues. They should be offered referral to a gastroenterologist and appropriate investigations and care.* *'Healthcare professionals and others should not confuse a difficulty eating due to ME/CFS-related gastrointestinal complications with psychologically based eating disorders.*	Thank you for your comment. The section on people with severe and very severe ME/CFS has additional recommendations on dietary management and strategies and includes referral to a dietician with a special interest in ME/CFS.

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				People with ME/CFS with difficulty eating should be treated with dignity and respect in accordance with this guideline, particularly the section 1.8 Access to Care.'	In the committee discussion in Evidence review G-non pharmacological management the committee note the importance of understanding the impact that ME/CFS symptoms can have on eating (in particular, resulting in weight loss and weight gain and that these are not necessarily the result of an eating disorder) and that any assessment should be undertaken by a dietician that has this understanding.
Science for ME (S4ME)	Guideline	034	021 - 029	Section 1.11.46 should be deleted. Too much information on CBT is provided here and in section 1.11 overall. There is no reliable evidence that CBT can treat or cure ME/CFS, or that it is effective for improving function in people with ME/CFS or supporting them to manage ME/CFS symptoms (evidence was rated low or very low quality for all CBT clinical studies, Evidence Review G, pp 72-119). Therefore, the extent of information provided on CBT is inappropriate. If it is offered as a supportive psychological therapy, it should be given no greater status than other psychological therapies.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). For this reason the recommendations you mention have not been removed. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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Science for ME (S4ME)	Guideline	034	002 - 005	The guidance not to offer CBT as a treatment or cure for ME/CFS is welcomed, but should be clearer. Suggested wording: '*CBT and other psychological therapies are not a treatment or cure for ME/CFS, or for the symptoms of ME/CFS, and should not be offered as such.*' The rest of this paragraph should be deleted. There is no reliable evidence that CBT is effective for supporting people to manage symptoms of ME/CFS. Quality of evidence for all outcomes across all CBT clinical studies included in the evidence review was found to be low or very low. This includes outcomes for physical functioning, quality of life, general symptom scales, and activity levels (Evidence Review G, pp.72-119).	Thank you for your comments. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). For this reason the recommendations you mention have not been removed.
Science for ME (S4ME)	Guideline	034	006 - 008	Should include recommendation to not refer people with ME/CFS to Improving Access to Psychological Therapies (IAPT) services, as IAPT therapists do not have appropriate training and experience in working with people with ME/CFS. (See Evidence Review G, p.326 lines 25-31.)	Thank you for your comment. The committee agree and it is clear in the recommendations that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS.
Science for ME (S4ME)	Guideline	034	006 - 008	Add that training and experience should be up-to-date and consistent with this guideline.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can

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					provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. For this reason your suggestion has not been added to the recommendation.
Science for ME (S4ME)	Guideline	034	016 - 018	The words '*recognises that thoughts, feelings, behaviours and physiology interact with each other*' should be deleted. This implies that the pathophysiology of ME/CFS can be altered by altering thoughts, feelings and behaviours, so symptoms can be altered using CBT. There is no reliable evidence for this. It is also virtually indistinguishable from the idea that abnormal illness beliefs or behaviours cause (or perpetuate) ME/CFS, which the draft states CBT for people with ME/CFS '*does not assume*'.	Thank you for your comment. This does not suggest that pathophysiology of ME/CFS can be altered by altering thoughts, feelings and behaviours it is a statement that thoughts, feelings, behaviours and physiology interact with each other. This the foundation of holistic care.
Science for ME (S4ME)	Guideline	034	025 - 027	This bullet point should be deleted. Language like '*establish strategies*' and '*work towards meaningful goals and priorities*' can be interpreted to mean that increasing activity will be feasible if strategies are put in place. This is not psychological support CBT, but CBT that aims to treat.	Thank you for your comment. The bullet point above explains that CBT is a collaborative, structured, time-limited intervention that focuses on the difficulties people are having at that time. The strategies and goals are directed by the person with ME/CFS. The next recommendation includes reviewing their plan regularly to see if their self-management strategies need to be adapted, for example if their symptoms or functioning change. The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment

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					and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Science for ME (S4ME)	Guideline	034	016 - 017	Should also include that 'abnormal' illness beliefs and behaviours do not perpetuate ME/CFS. Suggested wording: *'does not assume that ME/CFS is caused or perpetuated by 'abnormal' illness beliefs or behaviours'*	Thank you for your comment. This bullet point is underpinned by the holistic approach this guideline adopts and is a statement that thoughts, feelings, behaviours and physiology interact with each other but clarifies that ME/CFS is not a result of 'abnormal' illness beliefs and behaviours.
Science for ME (S4ME)	Guideline	034	001	Comment on the subsection 'Psychological support: cognitive behavioural therapy' We recommend the subsection 'Psychological support: cognitive behavioural therapy' (1.11.43 - 1.11.50, pp.34-35) be deleted in its entirety from the section 1.11 'Managing ME/CFS'. A shorter subsection on psychological support should be created in the section 1.6 'Information and support' after the parts headed 'Communication' and 'Information about ME/CFS'. This new subsection should include basic general information on psychological support, and clear statements that CBT should not be offered to treat, cure or support people to manage their ME/CFS or the symptoms of ME/CFS, as detailed below. Rationale for deletion of this section in its current form: 1. There is no reliable evidence for the effectiveness of CBT to treat, cure, or improve the functioning of people with ME/CFS, or to support them to manage ME/CFS symptoms. The section makes repeated inappropriate reference to CBT to support people to manage ME/CFS symptoms and improve functioning. Quality of effectiveness evidence for all outcomes across all CBT studies included in the evidence review was found to be low or	Thank you for your comment. After considering the range stakeholder comments on this section the committee edited the title to remove psychological support recognising this section only referred to CBT. After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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				very low. This includes outcomes for physical functioning, quality of life, general symptom scales, and activity levels; and comparisons of CBT with usual treatment and other interventions (Evidence Review G, pp.72-119, p. 318 line 23). 2. Reference in this section to supporting people to manage ME/CFS symptoms and 'improve functioning' conflates psychological support, with which the section purports to concern itself, with CBT to treat ME/CFS. This will lead to confusion resulting in CBT being offered to treat ME/CFS, therapists exceeding their expertise and resultant harm to people with ME/CFS. In discussing why benefits to quality of life and psychological status were not demonstrated in the clinical effectiveness evidence the Committee suggested there may be 'summative benefits' across other study outcomes including physical function, fatigue and activity levels, that 'may lead to longer term improvements in quality of life and psychological distress' (Evidence Review G, p.326). There is no reliable evidence for such 'summative benefits'. Assumptions based on qualitative evidence (which should be interpreted with caution) are not an adequate basis for including recommendations that CBT may be offered to support people to manage symptoms of ME/CFS or improve function or quality of life. (Evidence Review G p.320 also points to the quality of the qualitative studies being moderate to very low.) 3. There is no evidential basis for referring solely to CBT to the exclusion of other forms of psychological support. Our members have expressed preference for general psychological support, which may be provided informally by a healthcare professional (HCP) in conjunction with medical care. However, we suggest that information on psychological support should be generic and not mention specific modes or therapies. 4. Qualitative evidence suggesting benefits of CBT (see	reviews G and H for the evidence and the committee discussion on these recommendations). *Structure of a ME/CFS specialist service* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised certain parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Treatment or cure*

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				Evidence Review G p.324) should be interpreted with caution. Our forum members report telling a therapist they feel better due to wanting to please them and wanting to feel hopeful, when in fact nothing had changed. Of the members of the ME Association (https://meassociation.org.uk/managing-my-me-me-association-publish-results-of-huge-survey-report/) responding to a survey on helpful therapies for ME/CFS in 2010, 50% felt that counselling could be useful whereas only 28% reported that CBT could be useful. 5. We propose a consultant-led approach to management of ME/CFS, in which support with energy management would be provided by a specialist nurse who would also assist with symptom monitoring and management. CBT therapists are not qualified to provide these aspects of care; to do so would exceed their expertise and risk harm to people with ME/CFS. Rationale for movement of the 'Psychological support' out of 1.11 'Managing ME/CFS': Coverage of psychological support should not be included in section 1.11 'Managing ME/CFS' because there is no reliable evidence that CBT can effectively support people to manage ME/CFS or its symptoms. Instead, brief coverage of psychological support should be included in section 1.6 'Information and support'. The proposed subsection on psychological support in 1.6 'Information and support' should explain that: 1. Practical care, such as ensuring family and carers understand the illness, assisting with discussions with an employer, helping the person gain financial assistance and putting them in touch with peer group support, is important in helping the person cope.	To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. *Co-existing conditions* The managing co-existing conditions of section of the guideline raises awareness that other conditions may coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.

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				Our members report that this reduces the likelihood that formal psychological support will be needed. 2. Informal support is an important part of routine healthcare interactions, and should be considered a relevant aspect of care by all healthcare workers. Medical health care professionals are often well placed to provide informal psychological support as they may have an existing relationship with the person with ME/CFS and their family that pre-dates illness onset and they may have a good understanding of the health issues the person faces. 3. CBT and other psychological therapies are not a treatment or cure for ME/CFS, or for the symptoms of ME/CFS, and should not be offered as such (1.11.43 p.34; Rationale and impact p.67). 4. There is no reliable evidence that CBT or other psychological therapies are effective for improving function in people with ME/CFS, or in supporting them to manage ME/CFS or its symptoms. All CBT clinical studies were judged to be of low or very low evidence quality, and for all outcomes there were either no findings of benefit (e.g., quality of life) or inconsistency of findings (e.g., physical function, general symptom scales, fatigue, pain). (Evidence Review G pp. 72-119, 323-324). 5. Psychological support should be arranged if requested by the person with ME/CFS. It may also include information on psychological support for people with ME/CFS together with their partners or family members to help them to collectively adapt to changes brought about by the illness. 6. If a person with ME/CFS develops a mental health condition, NICE guidance for that condition should be followed. Grief, sadness, frustration and anger are normal reactions to the losses caused by ME/CFS; care should be taken to distinguish these	

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				from mental health conditions. HCPs providing psychological support for comorbid mental health conditions should have up-to-date ME/CFS training in accordance with this guideline to ensure that proposed treatment approaches to such conditions take the post-exertional malaise and other limitations particular to ME/CFS adequately into account in order to avoid harms. 7. Those providing supportive psychological therapies should have experience of ME/CFS and have training in accordance with this guideline. They should understand the constraints imposed by ME/CFS, and that the cause of ME/CFS is not understood, but there is no evidence that it is caused or perpetuated by deconditioning or faulty thoughts or behaviours. We provide comments on each recommendation in support of our suggestion to delete the subsection 'Psychological support' and include a shorter subsection on psychological support in 1.6 'Information and support'. These comments should also be considered as standalone feedback.	
Science for ME (S4ME)	Guideline	034	004	The term 'distress' should not be used. This assumes psychological distress that may not be present. Finding chronic illness difficult is a normal response to the debility and unwellness it entails, but 'distress' suggests more than this. Use of the term 'distress' throughout the draft guideline is further discouraged due to existence of the concept 'Bodily distress disorder' (ICD-11) which may inappropriately capture a subset of ME/CFS patients. The guideline should not use terminology that creates overlap with unrelated disorders focused on distress at bodily symptoms.	Thank you for your comment. Psychological distress has been deleted from this recommendation and in recommendation 1.12.29 has been edited to clarify that CBT aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
Science for ME (S4ME)	Guideline	034	005	After 1.11.43 add a recommendation: *'The risks of undergoing a course of CBT should be explained to people with ME/CFS of all severity levels, including that the physical cost of the interaction required to engage in the process may outweigh any perceived benefits. The cognitive and physical exertion involved may cause deterioration even for people with mild ME/CFS.'*	Thank you for your comment. It is important for the risks and benefits to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT

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					for ME/CFS. They will be aware of the risks that you highlight. For this reason your suggestion has not been added.
Science for ME (S4ME)	Guideline	034	010	The words *'manage the impact of [symptoms]*' should be deleted. There is no reliable evidence CBT is effective for this and the draft guideline acknowledges CBT is not a treatment or cure for ME/CFS (1.11.43, p.34; Rationale and impact, p.67). Quality of evidence for all outcomes across all CBT clinical studies included in the evidence review was found to be low or very low. This includes outcomes for physical functioning, quality of life, general symptom scales, and activity levels (Evidence Review G, pp.72-119).	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. For these reasons the words, 'manage the impact of symptoms has not been deleted.'
Science for ME (S4ME)	Guideline	034	014	The words '*aims to improve functioning*' should be deleted. There is no reliable evidence that CBT can improve functioning in ME/CFS. Only treatments of ME/CFS or its symptoms would improve functioning. The draft guideline acknowledges CBT should not be offered as a treatment or cure for ME/CFS (1.11.43, p.34; Rationale and impact, p.67). Further, this clause is likely to encourage therapists to operate outside the bounds of	Thank you for your comment and information. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a

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				their expertise, risking harm to people with ME/CFS. Quality of effectiveness evidence for all outcomes across all CBT studies included in the evidence review was found to be low or very low. This includes outcomes for physical functioning, quality of life, general symptom scales, and activity levels (Evidence Review G, pp.72-119).	chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. As part of this the aim of CBT is to improve quality of life, and this includes functioning and some of the evidence supported this (see evidence review G). . *Risks.* This is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks for the person and able to ensure the person with ME/CFS makes an informed choice.
Science for ME (S4ME)	Guideline	034	014	The term 'distress' should not be used. This assumes psychological distress that may not be present. Finding chronic illness difficult is a normal response to the debility and unwellness it entails, but 'distress' suggests more than this. Use of the term 'distress' throughout the draft guideline is further	Thank you for your comment. After considering the stakeholder comments, 'psychological' has been deleted to ensure it is not interpreted as this.

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				discouraged due to existence of the concept 'Bodily distress disorder' (ICD-11) which may inappropriately capture a subset of ME/CFS patients. The guideline should not use terminology that creates overlap with unrelated disorders focused on distress at bodily symptoms.	
Science for ME (S4ME)	Guideline	034	030	Recommendation 1.11.47 should be deleted. Too much information on CBT is provided here and in section 1.11 overall. There is no reliable evidence that CBT can treat or cure ME/CFS, or that it is effective for improving function in people with ME/CFS or supporting them to manage symptoms (evidence was rated low or very low quality for all CBT clinical studies, Evidence Review G, pp 72-119). Therefore the extent of information provided on CBT is inappropriate. If it is offered as a supportive psychological therapy, it should be given no greater status than other psychological therapies.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). For this reason the recommendations you mention have not been removed. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness.

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Science for ME (S4ME)	Guideline	034	030	The wording 'CBT for ME/CFS' suggests there is a particular kind of CBT that is effective and suitable for people with ME/CFS. There is no reliable evidence for this (evidence was rated low or very low quality for all CBT clinical studies, Evidence Review G, pp 72-119). It is important therapists working with people with ME/CFS have up-to-date ME/CFS training consistent with this guideline, but psychological support for people with ME/CFS (as for any chronic illness) does not require a special kind of CBT.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). *Up to date training* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
Science for ME (S4ME)	Guideline	035	023 - 026	Evidence Review G (p.328 lines 38-39), states, '*The committee noted that none of the evidence [on CBT] included or reflected the needs of people with severe or very severe ME/CFS.*' Therefore the guideline should recommend that people with severe or very severe ME/CFS should not be offered supportive CBT for ME/CFS, and particularly not CBT that is geared '*to support them in managing their symptoms of ME/CFS*', or to improve function, as there is no evidence of benefit but significant risk of harms.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline.

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					Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agreed that it was important that CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Science for ME (S4ME)	Guideline	035	023 - 026	Include that *all people* with ME/CFS are likely to struggle with the cognitive and physical effort of psychological support sessions and will benefit from shorter, less frequent sessions and longer-term goals. People severely affected by ME/CFS are likely to struggle greatly with the physical and cognitive effort, or be completely unable to undertake it. Strategies such as communication by email may help. Add: *'Risk assess any proposed course of CBT or other formal psychological support for a person with severe or very severe ME/CFS in advance to ensure that perceived benefits outweigh the risks to the person (for example, worsening their symptoms).'*	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments or focusing for periods of time can be difficult, and particularly so for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.

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					The committee agreed that it was important that flexibility in accessing CBT should be available for all people with ME/CFS but that is was important to highlight the additional caution needed for people with severe or very severe ME/CFS. The recommendations on the awareness of severe or very severe ME/CFS and its impact include that interactions should be risk assessed in advance to ensure its benefits will outweigh the risks to the person.
Science for ME (S4ME)	Guideline	035	005 - 007	What examples of self-management strategies are envisaged to be appropriate in a course of CBT for a person with ME/CFS? These lines should be deleted. There is no reliable evidence that CBT helps with people with ME/CFS's functioning and quality of life, including their sleep, activity or rest. Quality of evidence for all outcomes across all CBT clinical studies included in the evidence review was found to be low or very low. This includes outcomes for physical functioning, quality of life, general symptom scales, and activity levels. For all outcomes there were either no findings of benefit (e.g. quality of life) or inconsistency of findings (e.g. including physical function, general symptom scales, fatigue, pain, quality of life). (Evidence Review G pp. 72-119, 323-324). Attempting to change functioning and activity is attempting to treat ME/CFS. The draft guideline specifies that CBT should not be offered as a treatment for ME/CFS (1.11.43, p.34; Rationale and impact, p.67). Further, this may encourage CBT therapists to operate outside their expertise, risking harm to people with ME/CFS. Unrefreshing sleep is required for suspicion of ME/CFS in this guideline (p.8, Box 1). It is not a 'secondary disability' or 'psychological effect' of ME/CFS as suggested in Evidence Review G (p.326 lines 18-22). Therefore, it is not appropriate to offer CBT to support people to manage sleep symptoms of	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE

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				ME/CFS, and there is no reliable evidence that this will lead to improvement for any outcome measure.	guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
Science for ME (S4ME)	Guideline	035	009 - 011	These lines should be deleted. It does not make sense to have a 'self-management plan' separate from a 'management plan'. CBT therapists lack the appropriate expertise to review management plans for ME/CFS which need to include medical management of physical symptoms alongside energy management. The ME Association reported in 2010, based on a survey of their members, that a psychologist or psychiatrist was the least preferred health professional to co-ordinate the management of a person's ME/CFS illness. 'Managing my ME' report | The ME Association (https://meassociation.org.uk/managing-my-me-me-association-publish-results-of-huge-survey-report/)	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
Science for ME (S4ME)	Guideline	035	015 - 017	If this paragraph is included in the guideline, the risks of CBT should be described. It should include recommendation to ensure that the child or young person does wish to have CBT as supportive psychological therapy, and is not simply appeasing a parent or healthcare professional. The draft guideline includes the acknowledgment that children may have experienced prejudice and disbelief about their illness (draft guideline 1.1.6, p.5). Young people with ME/CFS have been harmed by CBT.	Thank you for your comment. The committee agree it is important for the risks and benefits to be explained and this is one of the reasons it is important that CBT is only delivered to people with ME/CFS by healthcare professionals with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. They will be aware of the risks that

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				Therapists should not contradict the child or young person's experience of ME/CFS, as views of the therapist are likely to be given more weight than the child's views. Therapists should not speculate about the cause of ME/CFS or pressure the child to increase any form of activity.	you highlight and be able to support the child or young person and their parents or carers to make an informed choice. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
Science for ME (S4ME)	Guideline	035	003 - 004	This bullet point should be deleted. This can be interpreted to invite therapists to encourage people with ME/CFS to invent and impose personal meanings on their symptoms and illness, increasing the likelihood unevidenced hypotheses on causes of ME/CFS may be applied. It creates scope for ill-informed therapists causing people with ME/CFS to feel blamed for their illness (See Evidence Review G, p.327, lines 8-15 on the importance of validation and non-blaming attitudes). There is no reliable evidence that such an approach is helpful and we think it poses a risk of harm to people with ME/CFS. Also, see Evidence Review G (p.325 lines 33-38) where noted experiences of CBT	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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				included perceptions of CBT as 'controlling, patronising and a form of brainwashing'.	reviews G and H for the evidence and the committee discussion on these recommendations).
Science for ME (S4ME)	Guideline	035	012 - 013	We question the need for a 'therapy blueprint' separate from the patient's management plan (medical care plan) and suggest this CBT tool has no place in the guideline for ME/CFS, as there is no evidence that dysfunctional beliefs have any role in causing or perpetuating ME/CFS.	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan. A therapy blueprint is specific to CBT, it is collaboratively developed between therapist and patient at the end of the course of therapy. The purpose of the blueprint is to summarise the course of therapy and strategies used, to provide a basis for future independent self-management and facilitate continued progress.
Science for ME (S4ME)	Guideline	035	008	This line should be deleted. It does not make sense to have a 'self-management plan' separate from a 'management plan'. The person's management plan needs to include medical symptom management as well as energy management, as each may impact the other. This requires the training of a doctor or specialist nurse. A CBT therapist is not qualified to assist the patient with the management of physical symptoms and medication.	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. If chosen by the person with ME/CFS delivered as part of the care and support plan and energy management plan.
Science for ME (S4ME)	Guideline	036	007 - 011	Add links to guidelines for postural orthostatic tachycardia syndrome (PoTS), Irritable bowel syndrome (IBS), gastroparesis, migraine and any other common comorbidities that have NICE guidelines.	Thank you for your comment. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not infer any importance of the condition in reference to co-existing with ME/CFS.

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					After considering the stakeholder comments the committee removed the reference to the NICE guideline on Coeliac disease and added the NICE guideline on irritable bowel syndrome in adults.
Science for ME (S4ME)	Guideline	036	005 - 006	This is an important point and needs emphasising. We suggest adding: Note that doctors need to be alert to the development of new comorbidities, and not assume new symptoms are part of ME/CFS even if they overlap with ME/CFS symptom lists.	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As noted this point is made in different sections in the guideline.
Science for ME (S4ME)	Guideline	036	005 - 006	Add: Be aware that people with ME/CFS may be more sensitive to drugs, and may need to start with smaller doses where possible, and some drugs may worsen ME/CFS symptoms. Be aware that treatments for coexisting conditions that include exercises may be contraindicated for people with ME/CFS.	Thank you for your comment. In the medicines for symptom management section of the guideline there is a recommendation that raises awareness that people with ME/CFS may be more intolerant of drug treatment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason you suggestion has not been added.
Science for ME (S4ME)	Guideline	036	012	Add: Care needs to be taken in diagnosing depression on the basis of questions about, for example, fatigue and lack of participation in social activities which may be caused by the patient's ME/CFS not by depression.	Thank you for your comment. This section links to the NICE guidance on co-existing conditions and does not any detail about the overlap of symptoms.

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					Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms.
Science for ME (S4ME)	Guideline	036	012	Add: Care needs to be taken to avoid misdiagnosing the natural healthy reactions of sadness and anxiety that occur when diagnosed with ME/CFS as mental health conditions. Acknowledgement of the severity of symptoms and practical support are likely in most cases to be more appropriate than a mental health referral.	Thank you for your comment. This section links to the NICE guidance on co-existing conditions and does not any detail about symptoms. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms.
Science for ME (S4ME)	Guideline	036	012	Add: If a comorbid mental health condition is diagnosed and the patient agrees to treatment, ensure that the provision of treatment and ongoing care is adapted to the limitations and needs of a person with ME/CFS, and provided by a professional with up to date knowledge of ME/CFS in accordance with this guideline.	Thank you for your comment. The first two recommendations in this section address this and advise that when managing coexisting conditions in people with ME/CFS, the recommendations in the sections on principles of care for people with ME/CFS, access to care and energy management should be taken into account.
Science for ME (S4ME)	Guideline	037	012 - 013	Add an extra point: '*Ensure this advice is discussed with patients in advance and included in their management plan (medical care plan), including who to contact for support and arranging extra care if needed.'*	Thank you for your comment. This is recommended in the assessment and care planning section of the guideline.
Science for ME (S4ME)	Guideline	037	001	Comment on section 1.13 Managing flares and relapses We find that the whole guideline, especially the management sections, focuses almost entirely on day-to-day management, and offers little, if any, information or guidance for clinicians or patients on dealing with the major life changes that most patients face. Apart from the sections specifically about severe and very severe ME/CFS, there is little recognition that those with moderate ME/CFS, which may be the majority of patients, face complete upheaval of their work, education and personal lives,	Thank you for your comment and information. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS.

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				as many are completely or virtually housebound, have difficulty accessing services, medical care and financial support. The impression is of minor adjustments, with family support available. That is not true for a large proportion of patients. Some of the sections for severe ME/CFS patients apply to those with moderate ME/CFS as well.	To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
Science for ME (S4ME)	Guideline	037	001	We suggest section 1.13 on managing flares and relapses should be part of, or come immediately after, the section on energy management, since it is an integral part of energy management with the same strategies of staying within the person's sustainable activity level, and making sure the person gets sufficient rest, according to their symptoms. Advice about energy management needs to include advice on how to manage any downturn, using symptom contingent pacing, whether it is a fluctuation, flare, PEM, PESE, relapse or prolonged deterioration. It is important that this topic be covered, as many new patients and doctors won't know what to do when symptoms worsen, but it is part of energy management, not really a separate issue.	Thank you for your comment. After considering the stakeholder comments on the structure of the guideline the committee agreed this was in an appropriate place in the guideline, links from the care and support plan and energy management recommendations have been added.
Science for ME (S4ME)	Guideline	037	002	Change the section title from '*Managing flares and relapses*' to '*Managing post-exertional malaise and prolonged deterioration*' The term flare is not one in common use, and in this context avoiding any mention of PEM seems perverse, since it is the most widely used term in diagnostic criteria, research papers and materials produced by patient organisations. Omitting it is likely to cause confusion. (we have suggested elsewhere that the terms flare and PESE should not be used in the guideline). We also suggest that 'relapse' may be misleading, as it is usually used in other conditions to refer to a recurrence of illness after a period of remission. In the case of ME/CFS, 'prolonged deterioration' may be a better way to describe what happens.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. The definition in the terms used in the guideline on flare up includes reference to PEM recognising that flare ups usually occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM. For these reasons the title of section has not been changed.
Science for ME (S4ME)	Guideline	037	009	Add: '*Complete bed rest may be necessary during episodes of PEM*' This is important, as many clinicians and family members don't understand just how sick people with ME/CFS can be with PEM.	Thank you for your comment. The recommendation includes general strategies for people with ME/CFS, specific strategies would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that

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					they cannot be exhaustive and there is the risk these are taken as the only options available.
Science for ME (S4ME)	Guideline	038	010 - 021	This implies that the person should discuss every worsening of symptoms with their clinician. This is unrealistic and, in many cases, unnecessary if the person is experienced in dealing with their fluctuations and PEM. Suggest adding starting the sentence with, 'If the person requests it, once an episode of PEM or deterioration...'	Thank you for your comment. The committee agree that not everyone will need a review of their care and support plans this recommendation is to check if this is the case.
Science for ME (S4ME)	Guideline	038	010 - 021	The phrase 'resolved or stabilised', and the rest of this section do not give sufficient emphasis to the fact that for many patients a period of deterioration leads to a very prolonged downturn to a greater severity level. It is important to emphasise that just advising making another 'Management Plan' (Medical Care Plan) on its own is insufficient. The logistics need to be organised in advance by the health provider for making a management plan (medical care plan) with a person who is too sick to attend a clinic, and may be too sick to cope with a home visit, and the talking involved, without further deterioration. Health providers need to ensure that services are available to ensure the management plan (medical care plan) can be implemented in a way that the person's health can tolerate, and is acceptable to the person. Flexible arrangements need to be in place, which the person knows in advance, with details of who to contact and how they can get help to cope with all aspects of their new situation, and to get the ongoing medical and home care they need in an accessible way. We feel it is important to spell this out in this section. The transition from mild or moderate to severe or very severe ME/CFS is likely to necessitate significant input from medical and care services, and these need to take into account the effects of any interaction on a patient with sometimes extreme sensory sensitivities, severe symptoms, and the serious effects of prolonged bed rest. The health and care professionals involved in making the new management plan (medical care plan) and assisting the person	Thank you for your comment. The committee recognise in recommendation 1.14.7 that in some cases relapses can last years and that during a relapse it may be necessary to review the person's care and support plan taking into account the symptoms and the severity and duration of the relapse. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. See the access to care section of the guideline and the care for people with severe and very severe ME/CFS. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.

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				in implementing it need to have up to date knowledge of severe and very severe ME/CFS in line with this guideline.	
Science for ME (S4ME)	Guideline	038	001 - 005	Add an extra bullet point: 'Explain to and recognise that for people with ME/CFS, particularly while experiencing PEM, and all the time for those who are severe or very severe, sensory stimuli (including sound, light and smells) and other environmental factors (e.g. temperature) can cause and worsen PEM and/or deterioration. Exposure need not be substantial or prolonged to cause significant worsening.'	Thank you for your comment. This section is about managing a flare up and relapse and the strategies to address this. The symptoms that people with ME/CFS experience are addressed throughout the guideline and in the severe and very severe section of the guideline.
Science for ME (S4ME)	Guideline	038	001	This makes it sound as though the patient needs to wait for agreement from a clinician before cutting back on activity during a relapse, which is unrealistic and inappropriate. Patients experiencing a prolonged deterioration (relapse) need to know in advance how to respond and who to contact for support if necessary. Suggested wording: '*During a period of deterioration, support the person in following the advice in their medical care plan*'	Thank you for your comment. This recommendation has been edited and makes it clearer that the strategies are discussed with the person and included in the care and support plan to help them respond promptly if they have a flare up or relapse.
Science for ME (S4ME)	Guideline	038	003	Delete 'even'. Patients whose condition deteriorates will need to cut back significantly on activities. This section is in danger of suggesting that only minor adjustments will be needed, when the reality for some is a step down to a significantly more severe level of ME/CFS.	Thank you for your comment. This bullet point reinforces that for some people stopping activities may be appropriate for this reason it has not been deleted.
Science for ME (S4ME)	Guideline	038	005	The wording here is unhelpfully vague and misleading. The use of a metaphor 'energy envelope' here is liable to lead to misunderstanding and overcomplicates the issue. It makes it sound as though the person has control over their 'energy envelope' and can manipulate it in order to stabilise symptoms. It also implies that some sort of planning or scheduling is possible. Realistically all the person can do is try to rest sufficiently to avoid further worsening. Suggested alternative wording:	Thank you for your comment. This has been edited to, 'reassessing energy limits to stabilise symptoms.' with the focus of the recommendation on reducing activity and resting. The committee hopes this adds further clarity.

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				'Recognise that the person will need to rest a lot more and ensure they have the support to enable them to do so. Advise them not to attempt to increase activity until symptoms improve sufficiently that the added activity does not lead to a worsening of symptoms.' We have proposed that the metaphor 'energy envelope' shouldn't be used, and plain language is preferred. The term 'symptom-contingent pacing' conveys in plain language that activity levels should be judged on current symptoms and the likely impact of activity on these, with the object of avoiding, and preventing further worsening during PEM and prolonged deterioration. This term can be clearly contrasted with potentially harmful forms of pacing, such as schedule-contingent or activity-contingent pacing. We are concerned that there is too much focus on working out envelopes and finding and recording new envelopes rather than on the key approach to preventing PEM and periods of deterioration, which is to rest as much as you need. If medical staff have any role during periods when symptoms have worsened, it is to be available in an accessible way to help with symptom relief if asked for, fit notes for employers, assist with getting care needs met, and reminding the patient to rest as much as they need to until they feel well enough to do more. There is an important role in helping the patient to give themselves permission to rest more than they feel they 'ought' to. Suggested additional point: "Ensure that the person with ME/CFS has, during PEM and periods of deterioration, • access to medical care for symptom relief,	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This section recommends that the person's named contact should be contacted if the person cannot manage the flare up or relapse using the self- management strategies in their care and support plan.

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				• if needed, fit notes and support for not returning to work or education until they can sustain the activity without causing worsening • if needed, additional assistance at home"	
Science for ME (S4ME)	Guideline	038	009	Add: If PEM does not start to resolve within the usual time for that person, or new symptoms appear, investigate other possible causes for worsening symptoms which may be mistaken for an ME/CFS downturn.	Thank you for your comment. The recommendation on what to review in the review section of the guideline includes that symptoms and any new symptoms should be discussed. After considering the stakeholder comments the committee have added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This is also reinforced with an additional recommendation this flare up and relapse section.
Science for ME (S4ME)	Guideline	039	002 - 004	This assumes the patient has a management plan. There is also a need to more clearly differentiate what care is appropriate in primary care and what requires specialist care. Replace the 'General' section with subheading 'Review of adults in primary care'. Replace 1.14.1 and 1.14.2 with 'Offer adults with ME/CFS: • a review of their care and management plan (if they have one) at least once a year • more frequent reviews as needed, depending on the severity and complexity of their symptoms and the effectiveness of any symptom management.	Thank you for your comment. The committee agreed it was important that all people with ME/CFS have care that is planned and supported by health and social care professionals working within a ME/CFS specialist team and made a recommendation that after confirmation of diagnosis by a ME/CFS specialist team a care and support plan should be developed. The committee hope this recommendation will ensure that all people with ME/CFS have a care and support plan. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) This title of the review has been edited to include primary care for clarification.
Science for ME (S4ME)	Guideline	039	023 - 025	This needs to be made firmer. As with any other patient, if the GP is concerned about a symptom and doesn't have expertise to deal with it, they should refer to the appropriate specialist, and not just to the ME/CFS clinic, which is unlikely to have the appropriate expertise either.	Thank you for your comment. The committee agree it is important that people with ME/CFS are seen by appropriate specialists when there is uncertainty in interpreting signs and symptoms and this recommendation

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				Replace with '*Do not allow the presence of an ME/CFS diagnosis to delay specialist assessment of signs and symptoms. Refer the person to an appropriate specialist to ensure prompt evaluation. Ensure any specialist involved in the care of the person has an up to date understanding of ME/CFS management in accordance with this guideline.*'	(1.15.5) is reinforced in the suspecting ME/CFS and diagnosis sections. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.. As the points you have made are clear in the guideline the changes you suggested have not be added to this recommendation.
Science for ME (S4ME)	Guideline	039	010	typo ME/CF should be ME/CFS	Thank you for your comment. This has been corrected.
Science for ME (S4ME)	Guideline	039	016	'activity management strategies' should be 'energy management strategies' to be consistent.	Thank you for your comment. This has been edited.
Science for ME (S4ME)	Guideline	039	018	Emotional and social well being should only be included if the patient wishes. It should not be assumed that all patients wish to discuss these.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning.
Science for ME (S4ME)	Guideline	039	021	Add a new subheading 'Review of adults in specialist care' Add: People should be offered a review by ME/CFS specialist care if:	Thank you for your comment. This section refers to review in primary care and recommendation 1.15.4 is clear that if there are any new or deteriorating aspects of their condition the person with should be referred to their named contact in the ME/CFS specialist team.

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				- there are any new or deteriorating aspects of their ME/CFS condition that cannot or have not been satisfactorily managed in primary care - they do not have a management plan and would like one - their ME/CFS severity is severe or very severe (in which case reviews more often than once a year are appropriate) Add: 'Where possible, people should have a named contact for ongoing specialist care, even if they do not currently require such care.'	The committee agreed it was important that all people with ME/CFS have care that is planned and supported by health and social care professionals working within a ME/CFS specialist team and made a recommendation that after confirmation of diagnosis by a ME/CFS specialist team a care and support plan should be developed. The committee hope this recommendation will ensure that all people with ME/CFS have a care and support plan. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) Recommendations 1.15.1 and 1.15.2 make it clear that reviews can be more than once a year according to the person's circumstances. As the points you make are clear in the recommendations no edits have been made.
Science for ME (S4ME)	Guideline	040	017 - 023	Replace first bullet point with: - provide evidence-based content and training methods compliant with this guideline (with input from people with ME/CFS) - Studies assessed as low quality or very low quality in this guideline should not be used to support training content. - Studies that suffer from the methodological limitations set out in p.317 of Evidence Review G should not be used to support training content	Thank you for your comment. The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The committee discussed the level of detail that should be included in training programmes and agreed on a general description to avoid a prescriptive interpretation of the content allowing the recommendations to remain relevant as research in the area develops. See evidence review B for detail of the committee discussion.

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				We do not think the phrase 'developed and supported by specialist services' is appropriate. This is because there are differences of opinions among care providers on what the evidence shows, and therefore there is a need to unequivocally state that training materials must be compatible with the guideline's recommendations. Many current service providers base their practice and understanding of ME/CFS on the CBT/GET model and its underpinning theories, and many still openly state their allegiance to that model. There are other groups with knowledge of ME/CFS that are better placed to develop and provide training than most current service providers. We are pleased that NICE have acknowledged the fundamental importance of patient involvement in the understanding of this disease and development of new training programmes. Ensuring training materials, including existing training materials, are compliant with the guideline and then delivering the training will be a major task. It must be adequately resourced and undertaken by those who approach ME/CFS in accordance with current evidence. The UK CFS/ME Research Collaborative (CMRC) education group is trusted by our members, is already producing training aligned with this guideline, and has good connections with experts in particular aspects of ME/CFS management. Add: • have been approved by the CMRC education group • are compliant with this guideline; existing training programmes that are not compliant should be withdrawn and reviewed, and only offered again when compliant with this guideline	We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme.
Science for ME (S4ME)	Guideline	040	012 - 015	ME/CFS is a relatively common serious long-term illness and yet health and care professionals typically currently graduate with little accurate knowledge of it.	Thank you for your comment. It is beyond the remit of NICE to recommend what should be included in undergraduate curricula.

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				Add: 'ME/CFS should be covered in the undergraduate medical curriculum, and postgraduate physician, paediatric and general practice curriculums. It must also be included in training for allied health professionals, nurses and others involved with health and social care.'	
Science for ME (S4ME)	Guideline	040	007 - 008	Since most paediatricians are unlikely to have up to date training in ME/CFS, and some who claim expertise currently promote GET or similar, we think it is important that this point emphasise that the GP needs to check whether the paediatrician has up to date knowledge of management of ME/CFS in line with this guideline. Add: 'Ensure any person involved in the care of the child or young person has an up to date understanding of ME/CFS management in accordance with this guideline before referring'.	Thank you for your comment. The first recommendation in this section has been edited to, 'health and social care providers should ensure that all staff delivering care to people with ME/CFS maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. '
Science for ME (S4ME)	Guideline	040	011	Comment on section 1.15 Training for health and social care professionals This new guideline presents a paradigm shift in the understanding of ME/CFS. It is essential that the recommendations are communicated urgently to clinical commissioning groups, specialist clinics, medical colleges and professional organisations of health and social care professionals, to prevent further harm.	Thank you for your comment. We hope the guideline will be read by these organisations when it is published. All registered stakeholders will be informed about the publication of the guideline.
Science for ME (S4ME)	Guideline	041	009 - 011	Activity Suggest adding: 'For people with very severe ME/CFS, significant activities include, for example, swallowing and listening to quiet speech'.	Thank you for your comment. **The definition of activity includes physical activity, the committee decided not to include examples of any activity (physical, cognitive, emotional or social) as any list of examples cannot be exhaustive and there is the risk these are taken as the only options available.**
Science for ME (S4ME)	Guideline	041	004	Add: 'These should include all professionals whose role impacts on people with ME/CFS, including clinical commissioners, employers, schools, housing providers, benefits assessors, safeguarding, clinical and care staff, clinical professional bodies and staff involved in assessing Long COVID patients.'	Thank you for your comment. It is clear in this section that the training recommendations apply to all health and social care staff that deliver care to people with ME/CFS and a list of professionals is not necessary. The remit of

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				This will need to be expedited as soon as possible alongside the production of the new guideline.	NICE does not extend to providing guidance for employers, schools, housing providers and benefits assessors but the committee would hope that any organisations who engage with people with ME/CFS would use this guideline as an example of best practice. Assessing Long COVID patients At this time the ME/CFS guideline and the COVID-19 rapid guideline: managing the long-term effects of COVID-19 address different populations. The key difference being the presence of post exertional malaise in people with ME/CFS. The COVID-19 rapid guideline: managing the long-term effects of COVID-19 includes a broader set of common symptoms and does not include post exertional malaise as a key symptom for diagnosis. While there is debate about the overlap between ME/CFS and the long-term effects of COVID-19 the development of this guideline started before the COVID-19 pandemic and the committee have only reviewed the evidence relevant to the scope. The long-term effects of COVID-19 is an area of research that is rapidly growing and it is inappropriate for this committee to comment or consider making recommendations that apply to both populations. NICE are developing and updating the COVID-19 rapid guidelines in order to reflect that evidence.
Science for ME (S4ME)	Guideline	041	004	Add: 'All services caring for people with ME/CFS need to be assessed for compliance with the new guideline's training requirements. This needs to be carried out independently, rather than as a service evaluation.'	Thank you for your comment. Assessing compliance with training is outside of the remit if NICE.
Science for ME (S4ME)	Guideline	041	005	Comment on section 'Terms used in this guideline' Explanation of terms used: The section 'Terms used in this guideline' states: 'Terms have been used in a particular way for this guideline'. We are concerned that new terms and new uses of terms will lead to misinterpretation when quoted and read out of context, or without reference to the definitions. We therefore	Thank you for your comment. When writing guidelines there is a judgement to be made about how much information to include and how detailed it should be. Too much information and detail results in a guideline becoming unwieldy and unusable. For this reason hyperlinks to definitions

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				think it vital that each term be defined in context, both at its first and any subsequent substantial use in the guideline. Hyperlinking is not sufficient.	are used to expand on a term that the committee agreed needed further clarity. The committee recognised that ME/CFS is area where many terms are controversial or disputed. This means where a term is used in a recommendation that the committee know can be interpreted differently it is important there is a definition clarifying what the committee meant by the term. However after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase or worsening of their symptoms. • *Debilitating fatigability.* This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Science for ME (S4ME)	Guideline	041	005	Comment on section 'Terms used in this guideline' Invention, redefinition and dropping of terms used: We question the appropriateness of NICE introducing or redefining terms. We think it more helpful, and evidence based, for current terms to be used, and defined according to common current usage in the literature and/or by patient organisations. We do not consider it	Thank you for your comment. The committee recognised that ME/CFS is area where many terms are controversial or disputed. This means where a term is used in a recommendation that the committee know can be interpreted differently it is important there is a definition clarifying what the committee meant by the term. However after taking into

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				is, or should be, the role of NICE to invent new terms or redefine terms differently from their use in the literature. The guideline does not exist in a vacuum. It will be referred to, quoted and read alongside other material by clinicians and patients. A new set of terminology not used elsewhere will create unnecessary confusion. This might be justified if the new terms and definitions provided greater clarity, but we have not found this to be the case.	consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase or worsening of their symptoms. • *Debilitating fatigability.* This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.
Science for ME (S4ME)	Guideline	041	005	Comment on section 'Terms used in this guideline' The term 'pacing' does not appear anywhere in the guideline. We have read the rationale for this in the supplementary material, but are not convinced by it. We feel it is unhelpful to omit mention of the term 'pacing' altogether, given its widespread current use, and sometimes misuse, in ME/CFS. The guideline does not exist in a vacuum. Patients and clinicians will come across 'pacing' in clinics and their publications, and material from patient organisations. We suggest it would be more helpful for pacing to be included in 'Terms used in this guideline', and 1.11 'Managing ME/CFS', with a clear explanation of the different versions in use and how they relate to the recommendations. We suggest the term symptom-contingent, (or symptom-based, or symptom-guided) pacing (recommended), and its contrast to schedule-	Thank you for your comment. The committee discussed the use of the term pacing and as you note agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.

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				contingent or activity-contingent pacing (not recommended), as being particularly helpful. Terms such as 'pacing up' (a version of GET) and 'adaptive pacing' (PACE trial structured version) need to be explained as unhelpful. Including explanations of these terms in the guideline may go some way to address the issue raised by the Committee of the range of interpretations and lack of a standard definition for the term 'pacing' (Evidence Review G, P.322). It is also important to make clear that the version of 'pacing' used in pain clinics is more like graded exercise therapy and should not be recommended for people with ME/CFS.	
Science for ME (S4ME)	Guideline	041	005	Comment on section 'Terms used in this guideline' We are not persuaded by the selection and definition of a mix of new and old terms used in the guideline to describe the effects of activity on symptoms and function. The terms used - energy envelope, fatigability, post exertional symptom exacerbation, post exertional malaise, flare and relapse are not clearly delineated. Nor are they defined in ways in common use in the literature or by patient groups. We are very concerned that this will lead to more confusion and misunderstanding of the effects of activity on people with ME. We suggest the following alternative simpler version: 'Energy envelope' be abandoned as a confusing metaphor, and simply described in plain language, as and when needed, as the amount of activity a patient is usually able to sustain on an ongoing basis without triggering significant worsening. 'Fatigability' be used to refer to the effect of increase in symptoms and abnormally rapid diminution in performance during and immediately after any and all daily physical and cognitive activity. 'PEM' (Post Exertional Malaise) be defined as the, often delayed, effect of activity beyond the person's capacity at the time, leading	Thank you for your comment The committee recognised that ME/CFS is area where many terms are controversial or disputed. This means where a term is used in a recommendation that the committee know can be interpreted differently it is important there is a definition clarifying what the committee meant by the term. After taking into consideration the range of comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. • *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. • *Flare to flare up*

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				to a significant increase in symptoms, and a significant reduction in function, lasting usually several days to weeks and sometimes longer. This version of PEM is in common use in some research, by some clinicians and by patient organisations. We recommend that Post-exertional symptom exacerbation ('PESE') be removed as unnecessary and leading to confusion. 'PESE' introduces untested terminology that health care practitioners will not be familiar with, may be misinterpreted as post-exertional fatigue experienced by people with some other conditions, and does not convey the increase in generalised unwellness and significant reduction in function that accompany other symptom worsening. We recommend the removal of the term 'flare'. It is unclear from the definition where 'PESE' and 'flare' would lie in relation to fatigability and PEM. 'Flare' is not in general use in the ME/CFS literature. Where it is used in the guideline we recommend it be replaced by a description such as 'worsening of symptoms' if it is meant in the general sense of any downward fluctuation, and 'PEM' or long-term deterioration for those specific phenomena. We recommend removal of the term 'relapse' as this is usually understood to mean deterioration after a period of improvement or remission which is not the common pattern in ME/CFS.	• *Relapse – the committee agreed not to change the term relapse.*
Science for ME (S4ME)	Guideline	042	014 - 024	Fatigability We are pleased to see this term spelled out separately from the usual 'fatigue' in diagnostic criteria. It should be defined as well as listing its key features, which should focus on the immediate and direct physical and cognitive effects. Delete lines 16-20 which are features of ME/CFS, not specific descriptors of fatigability. Suggested alternative definition: Fatigability is the increase in symptoms and abnormally rapid diminution in performance that occurs during any physical or	Thank you for your comment. After considering the range of stakeholder comments the committee have edited the definition fatigability to, ' Fatigue Fatigue in ME/CFS typically has the following components : • feeling flu-like fatigue, especially in the early days of the illness

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				cognitive activity, often with an abnormally slow recovery period after stopping the activity. Symptoms of fatigability include: • rapid muscle fatigue in which strength or stamina are lost quickly after starting an activity, causing sudden weakness, clumsiness, lack of coordination, and being unable to repeat physical effort consistently. The sensation of being 'physically drained'. In some cases, accompanied by increasing muscle pain. • cognitive fatigue that slows and worsens cognitive function.	• restlessness or feeling 'wired but tired' fatigue, or restless fatigue • low energy or a lack of physical energy to start or finish activities of daily living and the sensation of being 'physically drained' • cognitive fatigue that worsens existing difficulties • rapid loss of muscle strength or stamina after starting an activity, causing for example, sudden weakness, clumsiness, lack of coordination, and being unable to repeat physical effort consistently.'
Science for ME (S4ME)	Guideline	042	025 - 029	Flare It is not made clear in what way flare differs from Post-exertional symptom exacerbation (PESE) and Post Exertional Malaise (PEM), or from the fluctuations in daily ME/CFS. Flare is not a term commonly used in the literature, or widely used as a specific term by people with ME/CFS. The term increases confusion and is redundant. We strongly recommend that it not be used in the guideline. Where 'flare' is used in the guideline we recommend it be replaced by a description such as 'worsening of symptoms' if it is meant in the general sense of any downward fluctuation, and 'PEM' or 'prolonged deterioration' (recommended term instead of 'relapse') for those specific phenomena.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse. In addition the committee added to the definition,' flare ups usually occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM.'
Science for ME (S4ME)	Guideline	042	004 - 006	Energy Envelope. We find the definition unclear. We recommend that 'Energy envelope' be abandoned as a metaphor many find unhelpful, and simply described in plain language, as and when needed, as the amount of activity a patient is usually able to sustain on an ongoing basis without triggering significant worsening. Further, 'energy envelope' is associated in ME/CFS literature with a particular approach to energy management that is not universally supported.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Science for ME (S4ME)	Guideline	042	007 - 009	Energy Management: We have recommended that the term 'energy envelope' should	Thank you for your comment.

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				not be used in the guideline. We recommend the introduction of the term 'symptom contingent pacing' as a more helpful approach to energy management.	After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to energy limits*. The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms.
Science for ME (S4ME)	Guideline	042	017 - 018	Remove the item about sleep. The sleep effects may be present even without any activity, so should not be listed as part of the fatigability definition. We don't know what 'hypervigilance during sleep' means, and 'tired but wired' may occur during the day and prevent sleep, and is associated more with episodes of PEM, rather than a daily symptom of fatigability.	Thank you for your comment. After considering the stakeholder comments this bullet point has been edited to, 'restlessness or feeling 'wired but tired'' and 'hypervigilance during sleep' has been deleted.
Science for ME (S4ME)	Guideline	042	016	Remove 'especially in the early days of the illness'. This does not conform with our members' experience. Many continue to have 'sick or flu-like fatigue' for decades. We question whether there is sound evidence to support this.	Thank you for your comment. The committee agree people with ME/CFS continue to experience feeling flu like and the definition does not exclude this. In the committee's experience this was something they came particularly aware of in the early days of their illness and distinguished this fatigue from other types of fatigue.
Science for ME (S4ME)	Guideline	042	021	Suggested rewording: 'cognitive fatigue that slows and worsens cognitive function.' Not all people have permanent cognitive difficulties, but most or all do experience cognitive fatigability.	Thank you for your comment. The committee agree, the bullet point does not infer that all people have permanent cognitive difficulties but that fatigue experienced by people with ME/CFS includes cognitive fatigue that worsens existing difficulties at that time.
Science for ME (S4ME)	Guideline	042	022	After muscle fatigue add '(accompanied by increasing muscle pain for some people with ME/CFS) '	Thank you for your comment. The examples are related to the loss of strength or stamina and as such pain has not been added.
Science for ME (S4ME)	Guideline	043	020 - 026	Orthostatic intolerance This definition confuses symptom and cause. Suggested replacement: '*Orthostatic intolerance means an increase in symptoms when upright, or an inability to remain upright. In some patients with*	Thank you for your comment. After considering the stakeholder comments the definition has been edited to, ''A clinical condition in which symptoms such as lightheadedness, near-fainting or fainting, impaired

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				ME/CFS, POTS or postural hypotension may be the cause of OI but it is not established that blood flow hypotheses explain all OI in ME/CFS.'	concentration, headaches, and dimming or blurring of vision, forceful beating of the heart, palpitations, tremulousness, and chest pain occur or worsen upon standing up and are ameliorated (although not necessarily abolished) by sitting or lying down. Orthostatic intolerance may include postural orthostatic tachycardia syndrome (a significant rise in pulse rate when moving from lying to standing) and postural hypotension (a significant fall in blood pressure when moving from lying to standing).
Science for ME (S4ME)	Guideline	043	003 - 008	Management plan We consider the term 'medical care plan' to be more appropriate than 'management plan'. The former makes it clear that it is a plan to deliver care. The term 'management plan' implies that the person with ME/CFS and their condition are to be managed. All uses of 'management plan' throughout the draft guideline should be changed to 'medical care plan.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
Science for ME (S4ME)	Guideline	043	014 - 019	Moderate ME/CFS Some of the points listed are symptoms of ME/CFS experienced at all severity levels, not specific to moderate severity. We wonder why these specific symptoms were singled out for inclusion in this definition. The definition would be clearer if it focused on the level of functional capacity.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	009 - 013	Mild ME/CFS This description of mild ME/CFS really only describes very mild ME/CFS.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.

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Science for ME (S4ME)	Guideline	043	002	'change in treatment' is unclear. It should be made clear that this does not refer to an ME/CFS treatment, since there are none.	Thank you for your comment. It is clear throughout the guideline treatment refers to symptom management.
Science for ME (S4ME)	Guideline	043	006	'Add - 'if wanted by the person with ME/CFS' after 'other assessments and plans'. The person with ME/CFS should retain control of plans for their life.'	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans. https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care.
Science for ME (S4ME)	Guideline	043	007	In defining the management plan (medical care plan) we suggest changing 'cognitive behavioural therapy' to 'psychological support'. There is no research evidence that people with ME/CFS find CBT the most helpful modality of psychological support - of those who want psychological support, many prefer counselling. Nor is there any evidence that CBT therapists are the most appropriate health professionals for helping patients with energy management. This is likely to be better done by a specialist nurse who can also discuss medications and other approaches for symptom management.	Thank you for your comment. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.
Science for ME (S4ME)	Guideline	043	011	Even with mild ME/CFS, people are unlikely to be able to sustain full-time work without accommodations and substantial assistance at home. They are likely to need to reduce employment or education to flexible working or part-time, with	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The

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				some or all work or study done mostly from home.	introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	013	change to 'rest on weekends to recover from the week'. We don't think the word 'cope' is appropriate as it has connotations of not coping emotionally	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	015	add 'and most people of moderate severity are housebound most or all of the time' after 'have reduced mobility'	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	016	Delete: 'may have peaks and troughs'. This applies to all levels of severity, we are not clear why it is specified here.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a

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					guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	018	Replace: 'need rest periods, often resting in the afternoon for 1-2 hours' with 'need several hours rest during the day'. The afternoon rest time is too specific, and not evidence based. It may be an artefact of misguided attempts at sleep hygiene advice limiting night time sleep.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	019	Delete. Poor quality sleep is a feature of all severity levels of ME, not specific to moderate ME/CFS, and is covered in symptom lists elsewhere.	Thank you for your comment. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations. The introduction to the definitions of severity acknowledges that the definitions are not clear cut and individual symptoms vary widely in their severity and people may have some symptoms more severely than others. It includes that the definitions provide a guide to the level of impact of symptoms on everyday functioning.
Science for ME (S4ME)	Guideline	043	027	Physical activity We agree that this is a good general definition of physical activity for the healthy population. It would be helpful to adjust the definition to recognise that even very minor movements can have great significance to a person with severe or very severe ME/CFS. We suggest adding at the end of the definition: *'For some people with ME/CFS, physical activity as trivial as cleaning teeth and a brief conversation can account for a substantial proportion of the daily activity level that is possible.*'	Thank you for your comment. The definition does include that, physical activity has a health benefit but in people with ME/CFS physical activity may make their symptoms worsen. The committee noted that the impact would vary in individuals with ME/CFS and agreed to leave the definition broad.

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Science for ME (S4ME)	Guideline	044	023 - 029	Relapse We recommend removal of the term 'relapse' as this is usually understood to mean deterioration after a period of improvement or remission. People with ME/CFS may not have experienced any improvement whatsoever prior to deterioration of their condition. We recommend a more appropriate term, such as 'long-term deterioration' or 'prolonged deterioration' be used instead.	Thank you for your comment. After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
Science for ME (S4ME)	Guideline	044	018 - 022	Post-exertional symptom exacerbation This new term Post-exertional symptom exacerbation (PESE) should not be used. We support the continued use of the well-recognised term 'post-exertional malaise' (PEM). There is a strong argument for including the word 'malaise' which has the specific medical meaning of feeling very unwell, and describes PEM well. Guidelines should work with available evidence, rather than inventing new terms. PEM is the term used in international ME/CFS research and it is the term used in a wide range of training and information resources. The given definition of PESE is non-specific and could easily be misinterpreted as the same as post exertional fatigue, since it does not specify which symptom or symptoms are exacerbated, nor does the term convey the key facts that during PEM the person with ME feels both much sicker and has much reduced ability to function. We suggest the following alternative definition: Post-exertional Malaise: When a person with ME/CFS exceeds the activity level they are currently able to sustain daily - either due to a single high energy activity, prolonged exertion, or the cumulative effect of activities with too little rest - this triggers an episode of post-exertional malaise (PEM). The onset of PEM may be delayed by 12-48 hours, and it lasts at least a day, usually several days to weeks or longer. A bad bout of PEM or series of episodes of PEM may be followed by a prolonged deterioration to a more severe level of ME/CFS.	Thank you for your comment. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms. *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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				The symptoms of PEM are: - a marked reduction in function, often confining the patient to bed; - 'flu-like' malaise, with additional symptoms such as nausea, loss of appetite, sore throat, headache, dizziness, and acute sensory sensitivities; - a marked increase in, or changes to daily symptoms such as orthostatic intolerance (OI) and disordered sleep; - marked increase in the symptoms of physical and cognitive fatigability; - profound exhaustion; - a reduced threshold for incurring further PEM.	
Science for ME (S4ME)	Guideline	044	017	As physical maintenance is concerned with mitigating deconditioning and its effects, a clear statement should be added that ME/CFS is not caused or perpetuated by deconditioning and physical maintenance will not treat or cure ME/CFS or its symptoms.	Thank you for your comment. *Physical maintenance* After considering the range of stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. The committee agreed this was very important for people with ME/CFS with prolonged limited mobility.
Science for ME (S4ME)	Guideline	045	011 - 016	Therapy blueprint We suggest this term be deleted. We question the need for a 'therapy blueprint' separate from the patient's management plan. We do not expect that most patients will need or want 'therapy' in order to manage their activity and symptoms, though they may want support and information about helpful resources and strategies for activity management. There is no evidence that this has to be provided by a 'therapist'. A specialist nurse may be more appropriate. The phrase 'therapy blueprint' only appears once in the guideline in a section we are recommending should be deleted. It is a CBT tool and as there is no evidence for dysfunctional thoughts having anything to do with the aetiology or pathogenesis of ME/CFS it should be removed.	Thank you for your comment. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose **of** explaining these would be included in the blueprint. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.

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Science for ME (S4ME)	Guideline	045	017 - 020	Unrefreshing sleep Delete the sentence: 'Unrefreshing sleep is described as a light sleep'. It is not evidence based, not described this way in any of the diagnostic criteria and does not reflect our members' experience.	Thank you for your comment. After considering the stakeholder comments, this definition has been edited to,' Unrefreshing sleep means that is non-restorative. Even after a full night's sleep people do not feel refreshed. People with ME/CFS often report waking up exhausted and feeling as if they have not slept at all, no matter how long they were asleep.' to aid further clarity.
Science for ME (S4ME)	Guideline	045	024 - 026	Diagnostic tests. We agree this is important.	Thank you for your comment.
Science for ME (S4ME)	Guideline	045	015	Delete 'goals for the future'. We consider it wholly inappropriate for people with ME/CFS to be encouraged to make and record goals for the future. ME/CFS is a serious chronic illness for which it is impossible to predict what goals, however small, might be achievable. This sets the patient up for failure. If what is meant is goals to more effectively manage their activity, get sufficient rest, or make more use of available help and support, then that should be specified.	Thank you for your comment. A therapy blueprint is CBT tool which summarises the work a therapist and patient have completed together. The definition describes examples of strategies that may have been useful for the purpose of explaining these would be included in the blueprint. CBT is included as it can be part of someone's care and support plan if they have chosen to use it in supporting them in managing their symptoms.
Science for ME (S4ME)	Guideline	045	023	Our members have suggested the following could be added as important areas of research: Assessments of severity; upright hours Epidemiology - increase understanding of gradual onset cases; illness trajectory Treatments - including dose response trials Tired but wired phenomenon Pain relief - how effective standard pain management strategies and medications are for the pains experienced as a symptom of ME/CFS, and whether there are treatments patients find more helpful Orthostatic intolerance - which investigations are appropriate and should be included in diagnostic and review assessments, for example, tilt table testing for POTS and orthostatic hypo- or hypertension.	Thank you for your comment. The research recommendations are developed from the evidence reviews and as evidence looking for assessments of severity, epidemiology, tired but wired phenomenon, orthostatic intolerance investigations were not reviewed the committee were unable to make research recommendations on these topics. *Medicines* The committee recognised the lack of research in medicines but did not identify any one medicine to prioritise for research and as such did not make any research Orthostatic intolerance Research recommendations can only be made where the evidence has been searched for within the guideline. The

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					treatment of orthostatic intolerance was not included in the scope of this guideline as a topic to consider, and therefore the committee were unable to make research recommendations on this topic.
Science for ME (S4ME)	Guideline	046	001 - 003	Core outcome set We agree this is important. We suggest adding: '*including objective measures and ones that can be automated such as wearable technologies and apps.'* We also think some current questionnaire-based outcome measures are clearly unfit for purpose and it is just as important that this be recognised and their use discontinued.	Thank you for your comment. The core outcome sets are developed with the expertise of patients, carers and professionals. For further information see https://cometinitiative.org/assets/downloads/COMET%20Plain%20Language%20Summary%20v4.pdf
Science for ME (S4ME)	Guideline	046	005 - 007	Diagnostic criteria Suggested wording: *'Case definition for clinical use: Research which of the existing case definitions is, pending the development of a biomarker, most appropriate for use in clinical diagnosis and should be used in future NICE guidelines.'* We note that the guideline committee have modified an existing diagnostic case definition (IOM -Institute of Medicine), making it more restricted, with cognitive difficulties mandatory for diagnosis, whereas the IOM criteria list cognitive difficulties as an alternate core symptom with orthostatic intolerance. We are concerned that this decision was based only on the experience of the small number on the guideline committee, not on peer reviewed research. This will result in the exclusion from ME/CFS diagnosis of people, including some of our members, who fit the IOM criteria and some other criteria, and who would benefit from being recognised as having ME/CFS and the management and care recommended in the guideline. Missing out on diagnosis may lead to harm through mismanagement.	Thank you for your comment. There is further information on the research recommendation for diagnostic criteria in evidence review D. These are indicators of the topic areas to consider and all NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted. Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would be no need for the committee to address this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review

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					B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS. The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion
Science for ME (S4ME)	Guideline	046	008 - 010	Self-monitoring management strategies We agree this is important. It would be worth adding '*that are manageable by people with very limited energy and cognitive problems*. And add '*including ways to track activity levels and symptoms, ideally automated, and requiring little or no subjective input, such as wearable technologies and apps'*.	Thank you for your comment. There is further information on the research recommendation on self- monitoring management strategies in the appendices of evidence review H. These are indicators of the topic areas to consider and all NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted.
Science for ME (S4ME)	Guideline	046	004	We suggest adding a further, and important, section: 'Recommendations of areas where further research is NOT justified' These would include: 1. Activity based therapies Treatment trials of activity or energy management that include fixed or flexible incremental increases in daily activity or exercise. It has already been demonstrated that these approaches do not lead to improved health or function, and that many patients report worsening symptoms. Inventing yet another variation on this approach should not be used to justify further such research. It would be unethical to undertake any research that includes risking pushing patients into significant deterioration as part of a treatment program, regardless of what	Thank you for your comment. This section highlights the areas for research.

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				physiological model it is based on. We recommend further that any such trials currently in progress should be discontinued, and any further funding agreed for such trials should be withdrawn. 2. Psychological therapies It has been established that psychological therapies such as CBT are ineffective in improving the health or function of people with ME/CFS. We are aware that some therapists in current practice are introducing variations such as Acceptance and Commitment Therapy as treatments. We recommend that this practice be discontinued, and further trials based on such therapies for ME/CFS not be funded. 3. The role of personality factors in ME/CFS onset, perpetuation and treatment resistance Our members review a regular stream of research investigating a range of personality flaws in people with ME/CFS. This research is almost always done extremely poorly and, while not finding any evidence of such predisposing flaws, generally manages to conclude with an inference that such flaws do exist and that further research of this type is required. Our members find this research offensive and stigmatising. Given that nothing of value has been produced from this type of research after years of effort, and research funds have been wasted and substantial harm has been caused, we ask that funders do not continue to support it. We recommend adding a note that any funding process should require that any submitted ME/CFS research proposal include a letter of support from a major UK patient charity.	
Science for ME (S4ME)	Guideline	047	001 - 003	Sleep management strategies While we agree that sleep is a problem for many people with ME/CFS, it should not be assumed that standard 'sleep management' strategies are appropriate or effective. This section	Thank you for your comment. The committee agree that it should not be assumed that standard 'sleep management' strategies are appropriate or effective and medication is included in the research recommendation (see

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				should include research into which sleep medications people with ME/CFS find most effective.	evidence review H- non pharmacological management appendices).
Science for ME (S4ME)	Guideline	047	004 - 006	Dietary strategies We do not think this section should be prioritised. People with ME/CFS have tried a wide range of diets and many eat very healthily, but it has no impact on their illness. While it is true that some people with ME/CFS have food sensitivities, these need to be treated on a case by case basis as a comorbidity.	Thank you for your comments. Dietary strategies were not identified as a key recommendation for research but in the committee's experience this was area people with ME/CFS often asked for advice about and there is little research available to support health care professionals in giving advice.
Science for ME (S4ME)	Guideline	071	010 - 014	Move the detail of naming to the terms section. There is no need to cover this in the context; instead it can just be noted that ME/CFS is the term now used for a condition that has also been called myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS). Lines 10-14 could then be replaced with: 'Although its pathophysiology is not yet understood, ME/CFS is a well-defined condition with the hallmark clinical feature, post-exertional malaise (PEM)'	Thank you for your comment. The committee agrees there is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
Science for ME (S4ME)	Guideline	071	013 - 014	Suggested wording: 'Many people with ME/CFS consider the name 'chronic fatigue syndrome' inaccurate and trivialising because symptoms include much more than fatigue, and because fatigue is often wrongly assumed to be the same as tiredness.' We suggest this change because the use of the words 'simplistic' and 'judgemental' are value laden words that are in danger of reinforcing stereotyping of people with ME.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive. The committee note that none of the currently available terms describing ME/CFS are entirely satisfactory.

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Science for ME (S4ME)	Guideline	071	020 - 021	Delete the sentence 'Everyday life for people with ME/CFS, their family and carers is disrupted and unpredictable'. Disrupted and unpredictable are not the best descriptors of ME/CFS and the context notes that the condition has 'personal, social and economic consequences' and a 'low quality of life'. Change 'unemployed' to 'too sick to undertake paid employment or formal education', to make it clear that it is ill heath, not idleness, that means they are not working.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Science for ME (S4ME)	Guideline	071	009	Context We recommend that the Context, currently placed near the end of the draft guideline, be moved to a more prominent position at the beginning. This would be in line with the multiple sclerosis guideline where the Context is on page 4. A lot of the information in it about how it affects patients is vital information that should be part of an introduction to the whole guideline, along with a clearer and more comprehensive list of frequently occurring symptoms and descriptions of severity levels, prevalence of each and level of function and needs of each. There is so little knowledge about ME/CFS among clinicians, therapists and patients that we really need a clear exposition of what it is and how it affects people at the start of the guideline. Otherwise inaccurate assumptions will be made.	Thank you for your comment. The format of NICE guidelines is now to have the context at the end of the guideline. This section is clearly labelled and easily accessed on the guideline website page.
Science for ME (S4ME)	Guideline	071	017	Remove the word 'complex'. It gives the false impression that patients are complex and difficult. The rest of the sentence is sufficient without it. Replace 'multi-system' with 'with symptoms affecting multiple body systems'. While it is clear that there are multiple symptoms, we don't have evidence of pathology on multiple systems.	Thank you for your comment. There is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. After discussing in detail the wording of this recommendation the committee agreed not to change multi- system and keep complex, to indicate ME/CFS is multifaceted and complicated. This does not imply that patients are difficult.
Science for ME (S4ME)	Guideline	071	019	Remove the reference to 'emotional wellbeing', it is adequately covered by 'quality of life'. Singling it out gives the misleading impression that people with ME/CFS are likely to need psychological therapy. This may divert from the more practical help needed, and give undue prominence to the provision of CBT or other therapy as a core part of ME/CFS treatment.	Thank you for your comment. This sentence has been edited in line with the rest of the guideline where emotional wellbeing is to ,' significant impact on a person's quality of life, including their psychological, emotional and social wellbeing'.

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Science for ME (S4ME)	Guideline	072	007 - 009	This acknowledgement of the harm that has been caused by lack of belief is welcome and needs to be emphasised in a more prominent position in the guideline, reinforcing the importance of the whole context section moving to the beginning of the guideline. It is not only that people with ME/CFS are dissatisfied with care and disengage from services. In many cases there are no adequate or appropriate services for them to engage with. Using the terms 'dissatisfied' and 'disengage' applied to patients can be misinterpreted as fussiness on their part. We suggest a change of emphasis from patients to putting the onus on providers. Often there is nothing suitable provided that patients can opt into, thus preventing equitable access to care. This is particularly vital for people with severe and very severe ME/CFS who need thorough understanding of and sensitivity to their needs.	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Science for ME (S4ME)	Guideline	072	007 - 009	Add: '*For some people with ME/CFS, the impact of disbelief has been far greater than dissatisfaction with care and disengagement from services. Disbelief from health and social care professionals about their condition and related problems has led to misdiagnosis with mental health disorders, inappropriate involvement of mental health workers, instigation of mental health proceedings and in some cases detainment under mental health law.*'	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Science for ME (S4ME)	Guideline	072	010 - 011	We appreciate the inclusion of the particular needs of children, but this section underplays the seriousness of ME/CFS. Add: '*Some children and young people cannot attend school at all and may be too sick to undertake any education at home. Misunderstanding about ME/CFS has led to families facing social services enquiries, accusations of child abuse or neglect, or FII, and threats of children being removed from families if they refuse for their child to undertake a prescribed therapy with poor or no evidence of effectiveness in very sick children.*'	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive.
Science for ME (S4ME)	Question from	1		1 (From this form)	Thank you for your comment and information. The guideline reflects the evidence for best practice. The committee

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	comments form	22	13	Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. Re-orientation of clinical care teams With the recognition that the CBT and physical rehabilitation approaches are ineffective, the work of existing ME/CFS clinics must change. It is no longer appropriate for ME/CFS clinics to be managed or run by teams trained in CBT, psychotherapy, health psychology, psychiatry or occupational therapy. There is no need for therapists to provide individual and group courses of multiple sessions based on a psychological and behavioural model. These will need to be closed down as no longer fit for purpose, and their staff redeployed. New physician led medically focused teams will need to be set up, modelled on, and possibly in some instances sharing some staff and facilities with, those provided for other chronic disabling physical diseases such as multiple sclerosis and Parkinson's disease, with specialist nurses whose skill set better qualifies them to assist ME/CFS patients with managing their condition including both energy management, symptom monitoring and treatment, as well as helping with arranging appropriate assistance for work, education, financial, social and personal care needs. Specialist services such as physiotherapy for those who need them will also need to be available. Increasing expertise in ME/CFS Training of these new teams will need to be led by people with experience of working with people with ME/CFS in a manner which is fully in accordance with the new guideline. There is likely to be very limited availability of such trainers. It would be completely inappropriate for the training to be led by current providers of services based on the old guideline. A transition phase	acknowledge that there is variation in the delivery of some of the recommended services across the NHS but do not agree that there necessarily has to be widespread closure of existing services. There are areas that may need support and investment, such as training staff and providing more flexible access to care , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				The transition to the new approach to ME/CFS is likely to be a challenging time for GPs too. They may have long-term patients who understand the implication of the new guidelines in much more detail than they do, and have high expectations that everything will change immediately. They will also encounter patients whom they need to diagnose with ME/CFS, but then not quite know what to do with them – 10-minute appointments aren't suitable for helping new patients learn even the basics of energy management, let alone how to cope with all the other aspects of the condition. Clinical Commissioning Groups (CCGs) will need to plan the transition phase, including support for GPs needing to manage new patients without a ready-made network of clinics or an experienced consultant to manage patients with more severe symptoms. Getting a specialist nurse service up and running quickly, with nurses fully trained in accordance with the new guideline, under the supervision of physicians with up to date knowledge of ME/CFS and the guideline, should be prioritised, as should the provision of up to date materials for patients about ME/CFS. Care of people with ME/CFS who have given up on the health system Past users of clinics based on the old CBT/GET treatments should be informed of the new approach to ME/CFS. This could allow those patients who have avoided interacting with NHS services to benefit from the improvements recommended by the new guidelines. Just as with any medication that is withdrawn, the NHS has a responsibility to recall patients for a review and transfer to the new medical care approach. Improved care of people with severe and very severe ME/CFS There needs to be a suite of services including specialist nurses delivering care by email, text or phone and able to advocate for	

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				their patients; as well as mobile medical services delivering care to the person's home. There is a need for specialist high dependency housing for the more severely affected patients. Nursing homes are rarely suitable, as the most severely affected patients have severe sensory sensitivities and cannot be adequately shielded in a nursing home. Similarly, hospitals should have provision for appropriate sensory shielded single rooms for severely affected ME/CFS patients who need inpatient treatment and care. Coordinated management and monitoring Provision of new services compliant with the new guideline will need to be monitored closely by a national body set up for the purpose, using a robust system of compliance checks and quality control and with power to close down and replace inadequate services. There will also need to be a requirement for harms monitoring by these new services going forward and parity of harms monitoring for non-pharmacological approaches to condition management. If trust is to be restored, wholesale change is needed, including new medically oriented teams and rigorous monitoring of the new services.	
Science for ME (S4ME)	Question from comments form	2 22	 13	2 (From this form) Would implementation of any of the draft recommendations have significant cost implications? Using health and social care professionals who have good knowledge of the reality of ME/CFS (especially for those with moderate to very severe ME/CFS), should halt the problem of disabling symptoms being mistaken for signs of abuse, neglect or mental incapacity. This will result in significant cost and resource savings relating to inappropriate child care proceedings or sectioning of adults who are unable to eat or function due to their severe symptoms.	Thank you for your comment and information. The NICE implementation team are assessing the resource impact of recommendations. We acknowledge that there is likely to be an increase in specialist resources required in some parts of the country in order to make the provision of care more equitable than it has been in the past. Commissioners will decide how best to implement this locally. We note that the recommendations do not emphasise continued involvement by the specialist team. Instead, the focus is on an initial assessment and management plan by the team. Follow up should continue to take place by the general primary care team.

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				There will need to be initial significant redeployment and retraining as the professions employed in ME/CFS teams are reoriented away from a psychotherapeutic and behavioural model to a medical and energy management model. This will involve some initial costs in redeploying existing staff and recruiting and training new staff. Investment in useful care of people with ME/CFS is fully justified on the basis of the severity and long term nature of ME/CFS. It should, in the long run, save NHS money that has, until now, been wasted on poorly co-ordinated diagnostic processes and often lengthy and ineffective therapies.	
Science for ME (S4ME)	Question from comments form	3 40	11	3 (From this form) What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) A National NHS initiative to update all Clinical Commissioning Groups (CCGs) about the new approach is needed. National training courses for all staff deployed to implement the new model of care should be provided both online and in person, and new information materials written for clinicians and patients. The leading professional bodies - the Royal Colleges, need to be brought on board with this, with their current outdated training modules removed and replaced by guideline compliant materials. We suggest the education group of the UK CFS/ME Research Collaborative (CMRC) should play a lead role in providing such materials, and should be provided with government funding to produce accredited training courses designed for consultants, GP's, specialist nurses, medical students and other allied health professions.	Thank you for your response. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme (

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				It should not be left to local CCG's to produce their own training and materials, as most will not have appropriate staff with up to date knowledge, and there is a real danger that they will resort to assuming current providers of ME/CFS services will be willing or able to change their practices. It would also reduce the cost of unnecessary duplication of effort. Once a few new services are set up and approved by the leading education groups listed above, they can be used as models of good practice. We recommend the Telehealth service provided by the Australian ME/CFS charity Emerge. Their Telehealth nurses may be able to offer advice and even training online to NHS counterparts.	
The Ehlers-Danlos Support UK	Evidence Review G	230	036	This narrative review states that people with certain co-morbid conditions, notably joint hypermobility and fibromyalgia, in addition to 'irritable bowel syndrome, endometriosis, depression, arthritis, sciatica and asthma' experienced more difficulties with exercise programmes. We believe that people with these and other co-morbid conditions need to be advised of their greater risk during consideration of any exercise programme being offered. This goes back to the initial assessment of patients referred to ME/CFS services, where we believe that an examination for evidence of joint hypermobility should be carried out, since such a high proportion of people with hypermobility conditions are undiagnosed. If an examination is not possible for whatever reason, the 5 point hypermobility questionnaire could be used, as this is validated against the Beighton score.	Thank you for your comment and information. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
The Ehlers-Danlos Support UK	Guideline	General	General	We welcome this new guideline on ME/CFS as a step change in the history of this illness. Rapid dissemination of the key messages from this new guidance to all healthcare professionals will be vital, especially in the context of the Covid-19 pandemic.	Thank you for your comment.

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The Ehlers-Danlos Support UK	Guideline	004	003 - 021	We welcome and recognise the new description of ME/CFS. This matches our experience of supporting people who have been diagnosed with ME/CFS long the way to being assessed for an inherited disorder of connective tissue. In particular, we note how the previous stigma and disbelief experienced by patients may affect their relationships with clinicians now and in the future. That lost trust must be rebuilt.	Thank you for your comment.
The Ehlers-Danlos Support UK	Guideline	005	005 + 013	We recognise and endorse the importance of taking time to build relationships and to review patients regularly. This has resource implications for both primary and secondary care, given both the medical complexity and the historical issues around loss of trust.	Thank you for your comment.
The Ehlers-Danlos Support UK	Guideline	008	005 - 009	We expect that GPs will need further detailed guidance to help guide them as to what is meant by each of these four points. This is too general to be implemented without more information and the time required to perform such a comprehensive assessment.	Thank you for your comment. The terms used in the guideline define further fatigue, post exertional malaise and unrefreshing sleep. The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. • . The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness.
The Ehlers-Danlos Support UK	Guideline	008	016	We are concerned that the phrase 'had a specific onset' could risk excluding those with a more gradual onset from a diagnosis. Whilst many people note an onset of symptoms triggered by an illness, injury, operation or stressful event, others have a more insidious onset. This wording could be clarified.	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong. This now includes

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					the cohort of people who develop symptoms gradually sometimes over months or even years.
The Ehlers-Danlos Support UK	Guideline	009	004	We would suggest the addition of tachycardia (and perhaps also hypotension) to this list of orthostatic features, as PoTS is a recognised associated feature of ME/CFS. This list comes across as rather subjective, whereas there is objective and measurable evidence of autonomic dysfunction in ME/CFS.	Thank you for your comment. As with all examples included in recommendations they are not intended or can hope to be an exhaustive list. The committee note that the definition of orthostatic intolerance linked to includes postural tachycardia and hypotension.
The Ehlers-Danlos Support UK	Guideline	010	009	We do not feel it is appropriate to expect GPs to communicate with a patient's education or training establishment. We believe GPs are unlikely to have expertise in the specifics of appropriate adjustments or adaptations, which are likely to be different for each individual child or young person.	Thank you for your comment. The committee disagree, early communication with schools and colleges is very important. This recommendation refers to children and young people with suspected ME/CFS and the assumption should not be final diagnosis is ME/CFS. This recommendation is to raise awareness in the short term and allows for further communication when the diagnosis is confirmed. At this stage the support to the child's or young person's place of education should be specific to their current circumstance and condition.
The Ehlers-Danlos Support UK	Guideline	010	020	We are concerned that 'advising' a patient to 'maintain a healthy balanced diet' without a recognition that there may be practical barriers to doing this may have negative consequences. Buying and cooking food from scratch requires considerable energy and may be beyond the capacity of a patient who does not have the support of others. There are also financial considerations, as the person may have suffered a significant reduction in income. Similarly, *advice* to 'rest as they need to' may also be inappropriate – take, for example, a single parent. We would suggest rephrasing to something like 'explore how the individual can be supported to …'.	Thank you for your comment. This section refers to a short time period (6 weeks) and for people that are suspected to have ME/CFS as such the advice here is general. The section does start by being clear that care should be personalised as such access to care would be considered by the healthcare professionals providing care.
The Ehlers-Danlos Support UK	Guideline	012	003	We suggest a full physical examination is also necessary and should specifically include an assessment of postural cardiovascular function, such as a stand test as well as looking for joint hypermobility and other physical signs of hereditary connective tissue disorders (e.g. skin elasticity, piezogenic	Thank you for your comment. Physical health is stated as part of the medical assessment*. As with all medical assessments clinical judgement should be used and appropriate to the person having the assessment.

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				papules, abnormal scarring and arachnodactyly). It is not reasonable to rely on the initial GP examination, which by necessity will be brief.	Full history has been replaced with medical assessment.
The Ehlers-Danlos Support UK	Guideline	017	008 - 019	We strongly support these statements regarding safeguarding of children with ME/CFS which we believe should help to reduce the number of inappropriate investigations of such families based on misunderstandings by professionals of this complex and difficult condition.	Thank you for your comment.
The Ehlers-Danlos Support UK	Guideline	018	015	Suggest replacing the word '*fear* of relapse..' with '*risks of inducing* relapse', as this is a reality not a perception.	Thank you for your comment. After considering the range of stakeholder comments this recommendation has been edited to, 'risk that their symptoms will worsen may prevent people from leaving their home'.
The Ehlers-Danlos Support UK	Guideline	019	001 + 020	Discussion with the patient is only step one. A written care plan should be considered prior to admission. It is then vital to ensure that all members of the hospital team are fully aware of the specific needs and plans. This may need, for example, signs on the room door to alert porters, cleaning or housekeeping staff to the plans and specific requirements for such people. Otherwise these staff may inadvertently cause harm.	Thank you for your comment. As you note these recommendations include discussing the person's care and support plan to plan any adjustments, the aim would be to communicate this information to the hospital and the ward staff.
The Ehlers-Danlos Support UK	Guideline	020	027 - 029	We know from interactions within our support services that adaptations such as a blue badge or walking aid can be lifechanging. Rather than supporting the public misconception that such interventions are used by people to avoid activity, they more often enable users to do so much more than they would otherwise be able to do. We strongly support this suggestion. These visible signs make a massive difference to people with invisible disabilities.	Thank you for your comment.
The Ehlers-Danlos Support UK	Guideline	022	010	This message of a balance between activities is so important. In our setting in which we support people with chronic fatigue associated with connective tissue disorders, we have seen families criticised when a child has seen friends at a weekend and then been unable to attend for a full school week. Social contacts, family life and educational needs must all be considered as important.	Thank you for your comment.

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The Ehlers-Danlos Support UK	Guideline	025	011	'relationships' here should perhaps specify caring responsibilities or perhaps 'family life'. Many people with ME are parents, which can cause a real conflict between fulfilling this unavoidable role as mum or dad without exceeding their energy envelope. It would be good to acknowledge this genuine difficulty.	Thank you for your comment. This recommendation (1.11.3) provides an overview of what should be included in a discussion when developing a plan for energy management. The beginning of the recommendation also includes, discuss, 'along with anything else that is important to the person'.
The Ehlers-Danlos Support UK	Guideline	025	015	The majority of people do experience fluctuations in the amount of energy they have each day. This should be acknowledged up-front in every 'energy management plan'.	Thank you for your comment. This is acknowledged in the first recommendation in the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
The Ehlers-Danlos Support UK	Guideline	028	020	The proportions of people who are helped, not helped or worsened by exercise should be specified.	Thank you for your comment. This point was to illustrate that the impact of a physical activity or exercise programme can vary and for this reason your suggestion has not been added.
The Ehlers-Danlos Support UK	Guideline	028	023	It is important to recognise that necessary activities of daily living, such as showering, shopping and cooking also constitute 'exercise'. Some activities, for example taking children to school, cannot be avoided.	Thank you for your comment. The committee agree that all of the person's activities should be considered when developing an energy management and if appropriate a physical activity plan.
The Ehlers-Danlos Support UK	Guideline	030	010	The experiences of people with ME/CFS who also have orthostatic intolerance (OI) are different from other people with OI. It is our view that each ME/CFS service should either have the capability to manage OI, or have links with specific specialist OI services which are aware of ME/CFS. Treatment for OI often includes structured exercise programmes which are discussed elsewhere within this guideline as inappropriate without specialist input from ME/CFS specialists.	Thank you for your comment. The managing co-existing conditions of section of the guideline recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
The Ehlers-Danlos Support UK	Guideline	030	015	We welcome the acknowledgement of orthostatic intolerance (OI) in ME/CFS, but are disappointed that other recognised commonly co-morbid conditions are not similarly mentioned in	Thank you for your comment.

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				this new guideline, specifically Ehlers-Danlos syndrome, hypermobility spectrum disorders and disorders of mast cell activation (MCAS). In the same way that management of OI can help to relieve certain symptoms, the recognition of these other conditions opens up treatment options as well as avoiding future harms. Examples here would be altered approaches to childbirth, surgery or physiotherapy in a person with undiagnosed EDS or the use of intravenous contrast media in someone with unrecognised MCAS, which can cause anaphylaxis. Hypermobility is commonly found in people with ME/CFS and can explain some of the additional features, such as chronic widespread pain. As the committee has discussed in Evidence Review 6, specific drug treatments may help individual patients. Making these additional diagnoses may help guide such individualised management plans.	The discussion section of Evidence review D- Diagnosis includes a list conditions that commonly occur in people with ME/CFS and has the examples you have listed.
The Ehlers-Danlos Support UK	Guideline	031	014	We note that sometimes people with ME are reacting to the excipients rather than the active drug, so different brands of the same medication may have different effects. It may be worth pointing this out here.	Thank you for your comment. The committee have included in the other considerations section of Evidence review F:Pharmacolgical management that it is important that medicines management is tailored to the person with ME/CFS and as a result could not provide detailed advice on how to manage intolerance.
The Ehlers-Danlos Support UK	Guideline	033	001	Historically, some people report being disbelieved when reporting food reactions to doctors. Some people, including children, with ME/CFS may react to foods but not have IgE-mediated food allergy. As long as the person is still eating a healthy diet, we believe it would be helpful to state that they may be supported in avoiding certain foods, as long as the reasons for this have been explored. For example, some people are histamine intolerant, finding that they develop symptoms if too much histamine-containing food is consumed. Similarly, gluten intolerance without having celiac disease is relatively common in this population. Part of building trusting relationships with patients involves believing their lived experience, even if it is outwith our previous medical knowledge.	Thank you for your comment. The evidence did not allow conclusions to make recommendations on any dietary strategies. The committee have made a recommendation to refer people with ME/CFS for a dietetic assessment if they have a restrictive diet.

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The Ehlers-Danlos Support UK	Guideline	035	021	It would be helpful to state again here that the child or young person (or indeed adult) can opt not to have CBT or to stop the course of CBT sessions at any time should they so choose. CBT should never be forced on someone of any age.	Thank you for your comment. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
The Ehlers-Danlos Support UK	Guideline	037	007	Some women report that cyclical hormonal fluctuations impact their level of symptoms (typically a worsening in the pre-menstrual phase). It may be worth including this as a possible cause of a flare, as this is another potential individual treatment target.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The Grace Charity for M.E.	Guideline	General	General	We welcome the removal of Graded Exercise as a recommended treatment	Thank you for your comment.
The Grace Charity for M.E.	Guideline	General	General	We welcome the removal of promoting CBT as a cure	Thank you for your comment.
The Grace Charity for M.E.	Guideline	General	General	We are concerned that the WHO ICD 10 (G93.3) classification of M.E. as a neurological illness is not mentioned anywhere in the draft report. Please can this be mentioned because adhering to the WHO is a legal requirement by the NHS	Thank you for your comment. The text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context.

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The Grace Charity for M.E.	Guideline	General	General	Not enough is made of pain as a symptom: it is one of the most distressing and disabling symptoms for a sufferer and is part of the name of the illness i.e. MYALGIC – muscle pain. The painkillers suggested in the NICE guidelines are powerful and sufferers can be very sensitive to drugs: this is why non-pharmaceutical treatments should be accepted if they help, e.g. supplements, as they are more gentle on the sufferer.	Thank you for your comment. Pain is identified as a symptom that is associated with ME/CFS and the committee agreed that pain is a common symptom in people with ME/CFS and is particularly intense in people with severe and very severe ME/CFS. *Pharmacological management* Pain relief was included as an intervention in the protocol for pharmacological interventions. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
The Grace Charity for M.E.	Guideline	049	019 - 020	We are concerned over the 4 symptoms which have been listed as 'key' symptoms (page 49): 1) debilitating fatigability,2) post-exertional symptom exacerbation, 3) unrefreshing sleep and 4) cognitive difficulties. Whilst these symptoms do exist in M.E. these above selected symptoms on their own could be misinterpreted as depression. As previously referenced in our point no.4 the letter M in M.E. stands for myalgic (muscle pain) so we would like to see muscle pain added to the key symptoms. (Many sufferers also have nerve pain and joint pain.) SPECT scans have shown that M.E.	Thank you for your comment. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms, particularly with the addition of PEM. Pain may be associated but is not exclusive to with ME/CFS, this was supported by the IOM diagnostic criteria (2015).

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				and depression are not the same illness. (De Costa 1995 Quarterly Journal of Medicine and Schwartz American Journal of Roentgenology 1994)	
The Grace Charity for M.E.	Guideline	066	008 - 009	The prejudice against supplements is unhelpful to sufferers. Whilst supplements may not be offered as a cure, the general attitude to them is disparaging. Supplements tend to be the main choice of treatment and are recommended by private doctors specializing in M.E. Our charity is in constant contact with M.E. sufferers and we know how important supplements are for many M.E. sufferers and how much they have genuinely been helped by them. Since 2007 we have conducted an ongoing survey Treatment Survey – The Grace Charity for M.E. where feedback has been that different supplements consistently help M.E. sufferers. Also, in Jennifer Brea's film Unrest (2017) she promotes supplements as helping her to recover from M.E. Scientific (not just anecdotal) evidence for supplements helping M.E. sufferers has been documented since the 1980's. During the 1980s Professor Behan (Institute of Neurological Sciences, Glasgow) demonstrated that essential fatty acids could be very helpful in treating fatigue syndromes and indeed he conducted a placebo controlled double blind trial using 'Efamol Marine' – a mixture of evening primrose oil and fish oil, with beneficial results. Professor Puri, who is a Professor at the MRI Unit, Hammersmith Hospital and also Head of the Lipid Neuroscience Group at Imperial College, London, has picked up on some of this work and had similarly good clinical results. The NICE Draft Guidelines, whilst no longer promoting CBT as a cure, nevertheless say that some have found CBT 'useful' (Line 1 page 68), whereas supplements appear to be slammed in the report. Whilst supplements need not be offered as a cure (Lines 8 &9 page 66), they should receive more credit inasmuch as some find them helpful.	Thank you for your comment. No evidence of clinical benefit was identified for supplements and the committee were not confidant in recommending any supplements(see evidence review F- pharmacological review). After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' Recommendation 1.12.24 recognises it is the person's choice to take vitamins or supplements but that this should be an informed choice with an awareness about potential side effects.

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The Grace Charity for M.E.	Guideline	071	011 - 012	The following statement is untrue and needs to be corrected: 'There is little pathological evidence of brain inflammation which makes the term ME problematic' (page 71 11,12). The following young women diagnosed with M.E. were all found in autopsies to have brain inflammation: Alison Hunter 1977-1996 (Australia) The authors from Alison's brain tissue examined in 2016 concluded that the likeliest explanation for Alison Hunter's decline and eventual death was a severe Q fever attack that infected her organs, causing brain and heart dysfunction; i.e. she had a post-infective fatigue syndrome (source www.healthrising.org) Sophia Mirza 1973-2005(UK) The inquest determined that she died of acute renal failure as a result of dehydration. A later examination of her spinal cord found "unequivocal' inflammation in her dorsal root ganglia. The doctors reported that: "The changes of dorsal root ganglionitis seen in 75% of Sophia's spinal cord were very similar to that seen during active infection by herpes viruses (such as shingles)." (source www.healthrising.org) In Sophia's neuropathology report 13/2/06 the conclusion was 'Definite pathological changes are identified in this spinal cord specimen in particular there is a dorsal root ganglionitis in three out of four dorsal root ganglia sampled.' (source www.sophiaandme.org.uk) Lynn Gilderdale 1977-2008 (UK) Lynn had ganglionitis which is an infection of dorsal root ganglia of her spine, typical for a neurological illness (source MEpedia (me-pedia.org) and One Last Goodbye by Kay Gilderdale Ebury Press Merryn Crofts 1996-2017 (UK) A post-mortem found low-grade inflammation of nerve roots and inflammation of the dorsal root ganglia. (www.healthrising.org)	Thank you for your comment. The context provides background information to the guideline and sets the scene for developing the guideline. The content is not meant to be exhaustive. The committee agrees there is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. The committee agree that none of the currently available terms are entirely satisfactory.

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The M.E. Trust	Guideline	General	General	As a member of Forward ME, we support the combined submission from the organisations it represents. We would also like to provide specific comments which reflect our position as the only ME/CFS charity offering clinical services and support to people with ME/CFS, their families and carers.	Thank you for your comment.
The M.E. Trust	Guideline	General	General	We welcome the tone and overall direction of the new guideline, in particular the recognition that Graded Exercise Therapy (GET) is not appropriate for people with ME, and that CBT should only be offered as a support in certain cases to help in managing symptoms and not as a cure or treatment for ME/CFS	Thank you for your comment.
The M.E. Trust	Guideline	009	017	Early diagnosis is vital to prevent exacerbation of symptoms by patients not being aware of advice on symptom management	Thank you for your comment. Based on the qualitative evidence and their experience the committee agree it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. After considering the range of stakeholder comments on the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS. In summary the edits are: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. These edits do not change the recommendations that people with suspected ME/CFS should be given advice in section 1.3

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The M.E. Trust	Guideline	011	007	There are few specialist ME Teams in the NHS. This needs to be addressed through training, organisational structure and financial investment.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as access to ME/CFS specialist teams, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. .
The M.E. Trust	Guideline	012	010	Developing a personalised management plan could be the function of a trained specialist nurse.	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section).
The M.E. Trust	Guideline	013	001	It is essential to ensure collaboration by the medical practitioner with the patient in the creation of a management plan	Thank you for your comment. The committee agreed and have recommended a personalised care and support plan. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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The M.E. Trust	Guideline	013	012	Home visits are essential for people with severe ME/CFS. Our experience is that the most severely affected are often the most severely neglected.	Thank you for your comment.
The M.E. Trust	Guideline	018	019	Home visits are essential for people with severe ME/CFS. Our experience is that the most severely affected are often the most severely neglected.	Thank you for your comment. The committee agree this should be an option for people with severe or ME/CFS.
The M.E. Trust	Guideline	022	013	The importance of a multi disciplinary approach to care cannot be underestimated. The ME Trust provides a multi disciplinary team including a doctor, nurse, physiotherapist, counsellor and chaplain to provide care for body, mind and spirit.	Thank you for your comment and information.
The M.E. Trust	Guideline	023	007	The role of named contact could usefully be fulfilled by a trained specialist nurse	Thank you for your comment. The committee discussed whether it was appropriate to name a specific nominated professional but concluded that the most appropriate professional may vary within and between across services and that this would part of local decision making.
The M.E. Trust	Guideline	024	001	Managing ME/CFS should be treated as for other chronic diseases. After diagnosis by a doctor, the key to management is a specially trained lead practitioner – consideration should be given to training specialist nurses to fulfil this role and co-ordinate the involvement of other healthcare professionals.	Thank you for your comment. This multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.
The M.E. Trust	Guideline	024	005	Management of ME/CFS should include continued support, often over a long period of time. Consideration should be given to the needs of families and carers, especially those with severe ME and/or children with ME.	Thank you for your comment. The committee agree that people with ME/CFS should have ongoing support and have made recommendations for monitoring and review in the guideline. In addition there are sections on supporting families and carers of people with ME/CFS.
The M.E. Trust	Guideline	034	001	We agree that CBT should not be offered as a cure or treatment for ME/CFS, but that it may have value in a limited number of cases to help manage symptoms which are largely caused by the fact of ME as a long term, chronic disease.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. In addition recommendation 1.12.29 has been edited to clarify that CBT aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
The M.E. Trust	Guideline	040	011	There is an urgent need for training of health and social care professionals to 1) reflect current knowledge of ME/CFS 2) demystify and debunk myths about ME/CFS 3) develop best practice in the management of ME/CFS and the care of patients, their families and carers. A specialist qualification should be developed for nurse practitioners to enable them to take the lead in the management of this chronic disease within General Practice.	Thank you for your comment. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. It is beyond the remit of NICE to recommend specialist qualifications.
The ME Association	Guideline	General	General	General comment – The ME Association welcomes the new draft clinical guideline on ME/CFS. We wish to express our appreciation to NICE for the decision to undertake this review and to the members of the guideline committee for the work that has transformed the guideline into a framework of NHS care that people with ME/CFS, families, health and social care professionals can all support. – It has been a long time coming, but initial reaction from the charity's members and the patient community has been positive and we echo this sentiment. While we welcome the general ethos and specific aspects of the new guideline, we would like to raise the following points in the hope that the published guideline will be more encompassing. – ME Association comment has also taken into account valuable feedback from the patient community. The	Thank you for your comment and feedback on the guideline.

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				extensive comments should be seen as a reflection of the level of interest in the NICE guideline and recognition of how vital it will be in delivering effective healthcare provision for people who are suspected of having the condition and for those who have lived with ME/CFS for many years. We hope that NICE and the guideline committee will be able to give this feedback fair consideration as part of the stakeholder consultation and we look forward to reading the final guideline in April 2021.	
The ME Association	Guideline	General	General	Healthcare professional involvement – It was a general concern that the guideline is not specific enough about naming the healthcare professional(s) who should lead or be involved in the care and support of people with ME/CFS. – It was felt that General Practitioners and Paediatricians for the most part should be capable of taking the lead on healthcare for people with suspected ME/CFS or who have a diagnosis of ME/CFS and should be named throughout as the nominated health professionals. – It would help both professionals and people with ME/CFS to know who is in charge of their care at the various points in the guideline e.g., before and during diagnosis, for referrals, ongoing symptom and illness management, home visits, and for regular reviews etc. – ME/CFS specialist services will be involved and may take the lead during referral for a confirmatory diagnosis of ME/CFS or for ongoing management advice, for help with mental wellbeing, and re-referral during periods of worsened health if appropriate. – Other healthcare professionals might be involved when referrals are necessary to confirm alternative diagnoses, to help confirm a diagnosis, or for alternate treatment advice.	Thank you for your comment. *MDT composition* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. In addition, the committee discussed the value of naming which professionals should be in a team and as you comment no list is ever satisfactory or agreed. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (see Evidence review I _Multidisciplinary care) The committee note that throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care

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				Social care professionals will be involved when GPs or specialist services support referrals to local authorities for social care for people with ME/CFS.	and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Named contact* This section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse.
The ME Association	Guideline	General	General	Covid-19 and ME/CFS Clinical Vulnerability – Include a note about possible post-viral fatigue syndrome (PVFS) effects for people who are struggling to recover from Covid-19 infection. – Include that people in this situation could be (and are being) diagnosed with ME/CFS and/or experiencing similar symptoms. – Include that people ME/CFS are clinically vulnerable to Covid-19 infection as this could lead to a significant relapse in their health and are eligible for the free flu vaccine because they have a chronic neurological condition. – Include that people with ME/CFS should therefore be eligible for priority treatment with Covid-19 vaccines. – Include that similar management approaches for those with Post-Covid and those with ME/CFS might be applicable e.g., energy management and refer to relevant sections of the ME/CFS guideline. Include reference to the development of a NICE guideline on Post-Covid-19: https://www.nice.org.uk/guidance/indevelopment/gid-ng10179	Thank you for your comment. The guideline was developed before the COVID-19 pandemic and the committee reviewed the evidence relevant to the key areas of the scope. The committee have not reviewed the evidence on COVID-19 and are not in a position to comment or make recommendations in this area either about the long term recovery from COVID-19 or the vulnerability of people with ME/CFS to COVID-19 and prioritisation for vaccines. A link to the now published COVID-19 rapid guideline: managing the long-term effects of COVID-19 has been added.
The ME Association	Guideline	General	General	Guideline implementation	Thank you for your comment.

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				– How can The ME Association help ensure that Primary and Secondary Care as well as Clinical Commissioning Groups are more responsive to the new guideline and its aims? – If effective implementation of the guideline does not happen and is not supported by a determined education programme then the positive developments may not be implemented in practice – to the detriment of current and future patients. – We are concerned that despite the generally positive guideline, General Practitioners in particular may not provide an appropriate level of support and understanding to people with ME/CFS, will be disinclined to make early and accurate diagnoses, to refer promptly to ME/CFS specialist services, or offer timely advice on appropriate symptom and illness management. – We are concerned that ME/CFS specialist services are not available in all areas of England, do not receive priority commissioning, may not comprise appropriate medical experts, and may not be willing to remove or adapt previous management practices e.g., with regard to the removal of graded exercise therapy. – We would like to see NICE encourage the NHS to use the appropriate SNOMED CT classification for ME/CFS as a neurological condition to enable monitoring and recognition across the NHS in England. – We are unsure of NICE's involvement in the rollout of the guideline, implementation, enforcement, and with the training of healthcare professionals, but it would be useful if these concerns were considered. The ME Association is willing to continue working with NICE and the NHS to improve healthcare provision and understanding for people with ME/CFS in whatever way it can.	The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. Your comments will also be considered by NICE where relevant support activity is being planned. To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context section of the guideline.
The ME Association	Guideline	General	General	Introduction – It was recognised as being very important that the new guideline carry an introduction similar to the current NICE	Thank you for your comments.

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				guideline on ME/CFS: https://www.nice.org.uk/guidance/cg53/resources/chronic-fatigue-syndromemyalgic-encephalomyelitis-or-encephalopathy-diagnosis-and-management-pdf-975505810885 – This would greatly increase the impact of the new guideline and the chance for positive recognition and implementation. – The introduction should include for example: 1. An explanation of the main terms as they are referenced in the WHO ICD-11 e.g., post-viral fatigue syndrome (PVFS), myalgic encephalomyelitis (ME), and chronic fatigue syndrome. 2. An explanation and definition of myalgic encephalopathy (ME) and why this might represent a better term due to the lack of convincing evidence for pathological inflammation. 3. Recognition of the neurological classification of PVFS/ME/CFS as a disease and/or medical condition in WHO ICD-11, NHS SNOMED CT, and by NHS England in its work on long-term neurological conditions: https://www.england.nhs.uk/ourwork/clinical-policy/ltc/our-work-on-long-term-conditions/neurological/ 4. That there is good research evidence of brain, muscle, immune and neuroendocrine dysfunction to support a neurological classification and recognition as such in the NICE clinical guideline. 5. Recognition that ME/CFS is a disability classified in the Equality Act 2010 and that people with the condition may be eligible for welfare benefits such as Universal Credit and Personal Independence Payment and that carers may be entitled to Carers Allowance. 6. ME/CFS is a relatively common medical condition affecting both adults, young people and children of any age or ethnicity.	The introduction section has been replaced with the context section at the back of the guideline and includes background information. The context is not intended to be exhaustive and sets the scene for developing the guideline. Many of things you have listed are included and commented on throughout the guideline and the discussions in the evidence reviews. To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3) has been added to the context. *Vaccines* The guideline scope was agreed before the COVID-19 pandemic and the key areas included were the most appropriate at that time. The committee review the evidence relevant to the key areas of the scope and the recommendations were developed based on evidence reviewed before the COVID-19 pandemic. The committee have not reviewed the evidence on COVID-19 and are not in a position to comment or make recommendations in this area about the vulnerability of people with ME/CFS to COVID-19 and prioritisation for vaccines. *Equality Act 2010* In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.

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				7. The risk of ME/CFS being greater among women than it is men and the greater prevalence among women when compared with men. 8. Black and minority ethnic (BME) communities are likely to be at greater risk of ME/CFS but are often underrepresented and underreported: https://bmcmedicine.biomedcentral.com/articles/10.1186/1741-7015-9-26 9. ME/CFS is major cause of childhood sickness absence from school: https://bmjopen.bmj.com/content/1/2/e000252.full 10. Precipitating factors for ME/CFS commonly include: – a post-viral fatigue syndrome (PVFS) that has not resolved and was initiated by a viral or bacterial infection (e.g., flu, glandular fever, respiratory tract infection, viral hepatitis, meningitis, etc., and potentially, Covid-19 or e.g., Coxiella burnetii/Q fever and bacterial meningitis etc.). – Less common triggers include certain vaccinations (e.g., hepatitis B), toxins (e.g., ciguatera poisoning), pesticide exposure (organophosphates) and major stressful life events. – In a minority, there may not be an identifiable precipitating factor, and the onset may then be more gradual. 11. ME/CFS can occur in several members of the same family. 12. It is a complex and chronic disease affecting multiple body systems although its pathophysiology remains unclear at this time. 13. The physical symptoms can be as disabling as multiple sclerosis, systemic lupus erythematosus, rheumatoid	

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				arthritis, congestive heart failure and other chronic medical conditions including cancer. 14. ME/CFS places a substantial burden on people with the disease, their families, and society as a whole. It has been estimated to cost the UK economy £3.5 billion a year: https://meassociation.org.uk/wp-content/uploads/2020Health-Counting-the-Cost-Sept-2017.pdf 15. ME/CFS is recognised medical condition. It is not an example of Medically Unexplained Symptoms (MUS), or a functional neurological disorder, a psychological or mental health illness. 16. Be aware there is no current treatment or cure (non-pharmacological or pharmacological) for ME/CFS. 17. Prognosis, Permanency, and Quality of Life for people with ME/CFS: include relevant information about illness duration for adults and children and the expected effect on QoL. 18. There is a general lack of epidemiological data for the UK, but evidence suggests a population prevalence of at least 0.2–0.4%. This means that up to 265,000 adults, young people and children might be affected. A general practice with 10,000 patients is likely to include up to 40 people with ME/CFS. 19. Many different potential aetiologies for ME/CFS – including neurological, endocrine, immunological, genetic, and infectious – have been and continue to be investigated, but the diverse nature of the symptoms cannot yet be fully explained. 20. People with ME/CFS are eligible for the free flu vaccine because they have an chronic neurological condition and the risk of relapse or symptom exacerbation from the flu warrants recognition of this eligibility. People with ME/CFS should also be eligible for priority Covid-19	

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				vaccinations for similar reasons. The ME Association leaflet on Flu vaccine explains the situation and it would greatly help to have this reflected in the new guideline: https://meassociation.org.uk/wp-content/uploads/The-Flu-and-Pneumonia-Vaccinations-2020-2021.pdf 21. ME/CFS comprises a range of symptoms that when combined cause a significant impact on a person's ability to function normally. These include post-exertional malaise, chronic fatigue, headaches, sleep disturbances, difficulties with concentration, muscle aches and weakness, and pain etc. (see diagnostic criteria below). 22. A person's symptoms may fluctuate in intensity and severity, and there is also variability in the symptoms different people experience at any one time. 23. ME/CFS is characterised by post-exertional malaise which causes an exacerbation of other symptoms and can be triggered by minimal activity. This raises especially complex issues in people with severe and very severe ME/CFS. 24. ME/CFS, as with other chronic illnesses where there is uncertainty about the cause and exact disease process, provides a challenge for healthcare professionals. However, it should not prevent early and accurate diagnosis, the provision of suitable care, continuing support, and accessible help in managing the condition. 25. ME/CFS can cause profound, prolonged illness and disability, which has a substantial impact on people with the condition – who may be left housebound or bedbound – and reliant on the care and support of others. 26. The condition can have a mild, moderate, severe, or very severe effect on a person's health and functional ability, and even those who are mildly affected will be unable to function normally and may still be unable to	

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				work or to take an active role in education (link to illness severity definitions). The recommendations in this guideline emphasise the importance of acknowledging the reality of ME/CFS, of early symptom recognition, making an accurate diagnosis, and working in partnership with people who have the condition on an ongoing basis to manage it in the best way possible according to best practice and individual need.	
The ME Association	Guideline	General	General	Symptoms for suggesting ME/CFS Box 1 page 8-9 – The following is a summary of the points we make later in the comments. – Recommend the title is changed to: Symptoms required for a diagnosis of ME/CFS. – Prefer the way that the current guideline (1.2.1.2) displays symptoms. Box 1 in the new draft guideline is not as clear as it could be. – It was felt that accurate descriptions for the main and associated symptoms were vitally important and likely to affect the ease with which the new guideline is implemented. – Diagnostic criteria will affect people with suspected ME/CFS *and* people who already have a diagnosis any change cause an existing diagnosis to be questioned for example. – We need to ensure any change to the required symptoms does not lead to unnecessary confusion among healthcare professionals or anxiety among people with the condition. – Post-exertional symptom exacerbation (sic)… can be immediate or delayed by hours or days… We recommend that the main symptoms required for a diagnosis of ME/CFS are shown as: **1.** A substantial reduction in the ability to engage in pre-illness levels of activity (occupational, educational, or social) that:	Thank you for your comments. *Title* The committee have not edited the title as it is clear in the recommendations that these are the diagnostic criteria for ME/CFS. *PEM* The committee note that post exertional malaise is usually described as delayed in onset with it typically delayed 12-48 hours after activity, but recognised that some people with ME/CFS report PEM in a reduced (or later) time and have added 'can typically' to the definition. To note after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS.

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				▪ lasts for more than 3 months ▪ is accompanied by fatigue/fatiguability that is: • often profound, • of new onset (not life-long), • not the result of ongoing or unusual excessive exertion, • not substantially alleviated by rest. **2.** Post-exertional malaise (PEM) – worsening of symptoms after physical, mental or emotional exertion that would not have caused a problem before the illness: ▪ PEM can be immediate or delayed by 12 to 48 hours. ▪ PEM often puts the patient in relapse that may last days, weeks, or even longer. ▪ PEM can be induced by sensory overload (light and sound). **3.** Unrefreshing sleep and sleep disturbances, which may include: ▪ feeling exhausted, flu-like, and stiff on waking. ▪ broken or shallow sleep and altered sleep patterns. ▪ sleeping too much or too little. ▪ vivid dreams and night sweats. **4.** Cognitive difficulties (sometimes described as 'brain fog'), including: ▪ problems finding words, temporary dyslexia, or dyscalculia. ▪ slurred speech and slowed responsiveness. ▪ short-term memory problems, confusion, disorientation, and difficulty concentrating or multitasking. 1.2.4 Page 9 Be aware that the following symptoms may also be associated with, but are not exclusive to, ME/CFS	Unrefreshing sleep After considering the stakeholder comments on the description of sleep symptoms the committee edited the bullet points to, 'unrefreshing sleep and /or sleep disturbance, which may include: • feeling exhausted, feeling flu-like and stiff on waking • broken or shallow sleep, altered sleep pattern or hypersomnia. The committee have also edited the definition in the terms used in the guideline section. The committee hope this has added some clarity for readers. The committee discussed the other symptoms you suggested should be on the list and they agreed to add gastrointestinal symptoms to the list and taste has been added to the list of heightened sensitivities. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that urinary symptoms, weight loss or visual disturbances should be included in the list of associated symptoms. The committee note that urinary symptoms are listed in the examples of differential diagnosis in evidence review D and appetite, weight gain and visual disturbances are highlighted in recommendations within the guideline with reference to the description of or the management of symptoms.

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				– We would refer the committee to the way in which the current guideline (1.2.1.2) states: 'one of more of the following symptoms' and then lists the symptoms commonly reported to be part of ME/CFS in addition to the 4 main symptom requirements (as above). – In the new guideline the list of associated symptoms do not form part of the diagnostic criteria and we feel strongly that they should. – Health professionals should be left in no doubt that a diagnosis can only be made if the 4 key symptoms are present *and* at least one or more of the associated symptoms i.e., a diagnosis should not be made without them. – We have rearranged the list of additional symptoms in order of what we believe is the more important and made them a requirement of the diagnostic criteria: **5.** At least one or more of the following symptoms: ▪ flu-like symptoms, including sore throat, tender glands, nausea, chills, and/or muscle aches. ▪ orthostatic intolerance and autonomic dysfunction, including dizziness, vertigo, palpitations, fainting, nausea on standing or sitting upright from a reclining position. ▪ pain, including pain on touch, myalgia, headaches, eye pain, abdominal pain, or joint pain without acute redness, swelling or effusion. ▪ heightened sensory sensitivities, including to light, noise, touch, smell, and taste. ▪ temperature hypersensitivity resulting in profuse sweating, chills, hot flushes, or feeling very cold. ▪ neuromuscular symptoms, including twitching and myoclonic jerks. ▪ intolerance to alcohol, or to certain foods, and chemicals.	

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				We would also like to see included in the list above, the following additional symptoms: ▪ irritable bowel syndrome (IBS), or IBS-type symptoms, frequent episodes of diarrhoea and bowel discomfort. ▪ urinary incontinence and/or an increase in urinary frequency etc. ▪ weight loss or gain and changes in appetite and nutritional intake ability. visual disturbances that can prevent or limit visual capacity and reading ability.	
The ME Association	Guideline	General	General	Exclusionary testing and co-morbidities – The guideline needs to be specific about the tests that can be done when a person presents with ME/CFS symptoms or when new or worsened symptoms are reported. – The current guideline provides a list of tests (1.2.2) and we feel if they are not a part of the new guideline, the risk in primary care of missing alternative explanations for symptoms is increased. – While a diagnostic test for ME/CFS is a continuing priority for research, exclusionary testing, a full and careful review of the patient's clinical history, listening to the patient, and adherence to the ME/CFS diagnostic criteria, should allow for a relatively high confidence in the ME/CFS diagnosis. – The draft guideline is not specific enough about diagnoses that can exist alongside ME/CFS. There are certain conditions which commonly exist e.g., Fibromyalgia, and should not prevent a diagnosis of ME/CFS being made. These co-morbidities should be listed in the guideline so that any risk of missed diagnosis or treatment for an underlying condition can be more effectively managed and not overlooked.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. The discussion section of Evidence review D- Diagnosis includes a list conditions that commonly occur in people with ME/CFS and has the examples you have listed.

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The ME Association	Guideline	General	General	ME/CFS Specialist Services – The draft guideline is less clear (1.5) on the composition and responsibility of ME/CFS specialist services than the current guideline (and the supplementary material)was when published in 2007. – There is a real concern that the existing clinical network of ME/CFS services in England is in decline as the introduction of Clinical Commissioning Groups has resulted in ME/CFS support being seen as less vital and people with ME/CFS receive either no specialist support or are directed to other general services. – We believe it is very important to have a network of ME/CFS specialist services that comprise experts in the condition providing multi-disciplinary care and who can be consulted about diagnosis and for help with illness management and for advice about coping with the condition. – We also believe the new guideline supports the need for ME/CFS specialist services, but we are concerned that the guideline might prove insufficient to support their commission especially in areas that do not currently have them. – We would suggest including the ideal composition of a specialist services team – that they should be physician-led (consultants with specialisms in neurology or immunology, or GPs with a special interest in ME/CFS) and supported by a team of experienced occupational therapists, clinical psychologists, dietitians, and physiotherapists etc. – Specialist services may need to make significant changes to the way in which they approach illness and activity management given the welcome move towards energy management and away from graded exercise therapy, and this includes the preparation and dissemination of appropriate information to people with ME/CFS.	Thank you for your comment. *Structure of a ME/CFS specialist service* The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner. *Commissioning of services* The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of

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				– There is still too much about cognitive behavioural therapy in the new guideline, when we feel this is only one tool available to psychologists to help people with ME/CFS learn to cope, adapt, and accept the condition, and when the NICE guideline review revealed the poor evidence base for its efficacy. – Specialist services should make every effort to deliver appropriate and tailored management advice in sessions that do not cost a person with ME/CFS too much in terms of effort and energy expenditure. Alternative arrangements should be considered, for example, remote learning and remote consultations. Some people with ME/CFS have had setbacks in their health after long (2 hour +) sessions and the necessary travel that attendance has involved. – We welcome (1.8.2) the note about not discharging patients from health services when they might be experiencing a period of worsened health but feel this should be applied to ME/CFS specialist services in particular. – We understand that ME/CFS specialist services have to consider the financial implications of providing care and therefore restrict the number of appointments a person with the condition might have, but (1.14.3) discharge from a specialist service can feel like a person is unsupported if Primary care fails in its duty to provide continuing care and this should be stressed in the guideline. – Re-referring to specialist services is welcomed (1.14.4) and should be made explicit in the guideline so that people do not feel abandoned. Re-referral represents an additional cost implication for specialist services but is a very necessary part of ongoing management and support. – Home visits are a welcome inclusion in the guideline but might represent a challenge to ME/CFS specialist services. – Although we are aware that several specialist services are able to provide home support to those severely and very	the recommended services across the NHS. There are areas that may need support and investment, such as access to ME/CFS specialist services, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed however it was not within the committee's remit to make specific recommendations on service design and delivery. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS. *CBT* The committee discussed the number of recommendations on CBT and after taking into account the range of stakeholder comments agreed that it was important to keep all the recommendations to ensure that people with ME/CFS are offered and receive CBT safely and appropriately.

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				severely affected, we are equally aware that most current services are not. Home visits for those in most need should be considered a priority for specialist services and appropriate provision granted by Clinical Commissioning Groups.	
The ME Association	Guideline	General	General	Home visits and appointments – Home visits (1.5.5) are a welcome feature of the guideline but might represent a challenge to primary care and to ME/CFS specialist services. – Although we are aware that several specialist services are able to provide home support to those severely and very severely affected, we are equally aware that most current services are not. – Patient feedback has consistently revealed that GPs are very reluctant to visit people with ME/CFS at home but when this does occur appropriately, it can make all the difference. – Providing home visits does represent a resourcing challenge to primary care and ME/CFS specialist services but is a priority need for people who are not ambulatory, are in need and yet may not require hospital admission. – It was also noted that the guideline places emphasis on suspected and newly diagnosed people with ME/CFS. Concern was expressed about the lack of support from – and contact with – primary care and specialist services for people who have had the condition for a number of years and who may not have an established relationship. – Can the guideline recommend that primary care proactively contact all people with ME/CFS and seek to establish a relationship? The SNOMED CT coding system should make it easier for primary care to determine who has a diagnosis of ME/CFS. This was felt to be very important although it could represent a challenge to primary care. – In certain circumstances it might be possible to provide remote consultations (telephone or video), but most people	Thank you for your comment. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as one of the examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agree that there is variation in the delivery of home visits across the NHS but these recommendations will provide equity of access for this group, particularly for people with ME/CFS who are have difficulty or are unable to leave their homes.. *People diagnosed with ME/CFS* The committee hope this guideline is applied to all people with ME/CFS. It is beyond the remit of NICE to recommend that all people with ME/CFS are contacted but the review section of the guideline recommends that adults should be offered a review of their care at least once and year and children and young people every 6 months. This section notes the minimum areas for review. *GP consultation time*

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				severely or very severely affected (in particular the latter where communication is especially difficult or impossible) will require ongoing home visits to provide continuity of care and medical or related support. – A related point is that people with ME/CFS should be afforded a longer period of time for a consultations with a GP if they are able to visit the surgery. The usual 10-minute appointment is an inappropriate period for people who might have used up considerable energy travelling to the surgery or who have cognitive challenges and difficulty communicating their needs. It is welcome that the guideline implies greater use of remote consultations, but these should be equally applicable to anyone with ME/CFS regardless of illness severity who is better able to telephone than to visit the surgery in person for example.	The committee are unable to recommend the length of appointment times but have recommended in the access to care section that Service providers should ensure people with ME/CFS can access health and social care services by adapting the timing, length and frequency of all appointments to the person's needs.
The ME Association	Guideline	General	General	Hospital Care – The recommendations and considerations relating to hospital care for people with ME/CFS and those severely and very severely affected are particularly welcome (1.8.1, 1.8.5, 1.8.6). – We question however how practical these measures might be when it comes to catering to a person's individual needs either as an outpatient or inpatient at hospital. – It has not always been practically possible – or financially possible – for ME/CFS specialist services to provide sufficient service that takes into account individual needs or even to provide home visits. – There are no hospital inpatient facilities for people with ME/CFS and hospital admission for e.g., unrelated surgery, does not always result in suitable measures to make a person with ME/CFS comfortable. – While it is appropriate to include these measures, it would help to have some idea of how likely it might be for them to occur. For example:	Thank you for your comment. The committee agree that access to services for people with ME/CFS is very important and have reinforced this throughout the guideline. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS including the provision of inpatient care for people with ME/CFS. There are areas that may need support and investment, such as access to ME/CFS specialist services, to implement some recommendations in the guideline. This guideline highlights areas where resources should be focussed however it was not within the committee's remit to make specific recommendations on service design and delivery. Commissioners are listed as one of the groups that the guideline is for and the committee hope that new guideline will be taken into account when commissioning services for people with ME/CFS.

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				o To what extent are ME/CFS specialist services able to adopt these measures on an individual basis? o Would admittance to hospital via ambulance likely take account of a person's needs? o Are there any hospital inpatient services who are able to cater to a person's needs? o To what extent can these measures be used by a person with ME/CFS to improve the way they are treated in hospital? o When a person with ME/CFS is admitted for surgical procedures will these measures be taken into account as well as measures relating to e.g., suitable anaesthetics? If these welcome measures were to be implemented effectively, it could result in a significant practical and financial challenge to the NHS, but this shouldn't prevent them from being undertaken.	
The ME Association	Guideline	General	General	Management – The changes to illness management (1.11) are in general welcome, but concern has been expressed about the exact nature of the 'energy management' and 'symptom management' approaches. – Can more detailed guides be produced that serve to support primary care and ME/CFS specialist services so that a more consistent approach to best practice is applied throughout the NHS in England? – This might help to ensure that people with ME/CFS receive the best advice possible which is then tailored to the individual. – It would also help primary care providers to know how management approaches should be applied and enable a more effective implementation of the guideline principals. It would be helpful if the production of any guides could involve ME/CFS charities and patient representatives before being distributed to the NHS.	Thank you for your comment. Evidence reviews G and H on non pharmacological management set out the evidence and committee discussion for energy management and symptom management and provide further information on these topics. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.

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The ME Association	Guideline	General	General	Symptom Management – We strongly recommend a new section titled: Symptom Management be created before the section about orthostatic intolerance (1.11.24). – Include that people with ME/CFS have found pharmacological treatments helpful for symptom relief and that physicians should consider appropriate options when in consultation. – In NICE Evidence Review F Pharmacological Management, page 94, lines 30-33 it says: – "The committee acknowledged that while there are not any current pharmacological treatments or cures for ME/CFS, people with ME/CFS have found some drugs when used appropriately with advice and support from health care professionals can be helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis." https://www.nice.org.uk/guidance/GID-NG10091/documents/evidence-review-6 – This comment should be included in the clinical guideline because we are concerned that without it, physicians will not consider potentially very helpful pharmacological treatments for symptom relief which could lead to avoidable suffering in some cases. – Symptom management should include all of the symptoms that relate to ME/CFS – as determined in Box 1 on pages 7-8 'Symptoms for suggesting ME/CFS' and the additional symptoms shown in section 1.2.4. – NICE should advise on the best approach for managing each symptom, including medications for symptom relief where appropriate, with links to other NICE guidelines if applicable e.g., Irritable Bowel Syndrome, and non-pharmacological options where these are known.	Thank you for your comment. After considering the stakeholder comments the *managing ME/CFS* section has been separated into two sections with orthostatic intolerance now included in the section *symptom management for people with ME/CFS*. Medicines for symptom management is included in the symptom management section of the guideline and medicines management is listed as expertise needed by people with ME/CFS indicating the importance of considering this for people with ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation. *Management of symptoms* Evidence reviews G and H on non pharmacological management set out the evidence and committee discussions for the clinical and cost-effectiveness of non-pharmacological interventions for people with ME/CFS. This sets out the rationale for the recommendations in the management of ME/CFS and the symptom management section. Where the committee were confident in making recommendations based on the evidence and using their expertise and experience they did. However there were areas where no evidence was identified and the committee were not confident in making a recommendation, for example cognitive difficulties.

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				– At present the guideline is significantly let down by the omission of these details and the focus on only three of the additional symptoms for ME/CFS: orthostatic intolerance, pain, and nausea. – Even where there are no specific symptom management options and people with ME/CFS are best advised to defer to general energy management and other techniques, it shouldn't prevent the inclusion of those symptoms in this section. – Including a section about symptom management would help to focus healthcare professionals on the need to consider and to provide additional help to support people trying to cope with symptoms. – Healthcare professionals should be directed to consider appropriate prescription medications where any exist, and other alternative options, that might provide symptom relief e.g., in the case of sleep problems or pain etc. We would refer the committee to the NICE clinical guideline on Multiple Sclerosis for a comparison (section 1.5): https://www.nice.org.uk/guidance/cg186/resources/multiple-sclerosis-in-adults-management-pdf-35109816059077	The NICE guidelines on Irritable Bowel syndrome (CG61) has been added to the list of co- existing conditions.
The ME Association	Guideline	General	General	Psychological support: cognitive behavioural therapy – Recommend that the title becomes 'Psychological support' or 'Mental health support' or 'Mental Wellbeing' and that 'cognitive behavioural therapy' is removed (1.11.43 - 50). – While we recognise the importance of psychological support for those people with ME/CFS who require it e.g., learning to accept, adapt, and to live with such a life-changing and debilitating medical condition, we do not agree that CBT should be the only recommended option in this guideline. – When the guideline committee reviewed the research evidence for CBT in ME/CFS, most studies were deemed to be of low or very low quality. This does not in our view support the headline recommendation for CBT.	Thank you for your comment. Taking into account the range of stakeholder comments the recommendations on CBT are now under the sub heading cognitive behavioural therapy and psychological support has been removed reflecting that the recommendations are only about CBT. The committee discussed the number of recommendations on CBT in this section and after taking into account the range of stakeholder comments agreed that it was important to keep all the recommendations to ensure that people with ME/CFS are offered and receive CBT safely and appropriately.

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				– CBT is a tool that a psychologist might use and adapt to the individual, but it is not the only tool they might employ. – We do not doubt the value of having access to a therapist who has experience of ME/CFS and who might be a key part of an ME/CFS specialist service. – It can be very helpful for some people with ME/CFS to talk to a professional who understands and is able to offer them a constructive outlet for their anguish and frustrations, who might help them learn how to cope with the often-crippling effects that this condition can have on a person's mental wellbeing. But we feel CBT should be removed as the headline therapy in the guideline and far less space should be given to it (although some of the advice is as applicable to psychological support in general).	
The ME Association	Guideline	General	General	Medical reviews – The guideline recommends a 12-month medical review (1.14.1). Regular reviews are welcome as no person with ME/CFS should be without regular contact from their GP and/or ME/CFS specialist service unless they decide such contact is not required. – We would suggest a review occur at least every 6-months and that GPs initiate contact with people who have ME/CFS, inviting them for a review which could be via telephone or video if either option is preferable. – 6-montly reviews were recommended for people with long-term conditions by NHS England and the NHS recommend 3-monthly reviews for people who are eligible for continuing healthcare due to complex needs. While we feel regular reviews are a priority – as is maintaining contact with NHS services generally – we recognise this could add to the financial burden experienced by primary care and ME/CFS specialist services.	Thank you for your comment. The recommendation is to offer a review at least once a year and the following recommendation to arrange more frequent reviews if necessary.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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The ME Association	Guideline	048 - 072	General	We have no comments to make about the rationale and presumed impact other than the comments above.	Thank you for your comment.
The ME Association	Guideline	008 - 009	Box 1	Symptoms for suspecting ME/CFS – Recommend the title is changed to: Symptoms required for a diagnosis of ME/CFS. – Prefer the way that the current guideline (1.2.1.2) displays symptoms necessary for a diagnosis of ME/CFS. – Box 1 in the new draft guideline is not as clear as it could be. – 'Debilitating fatigability' is a new and uncertain term, although the linked definition is good. – There is potential confusion between '*not* caused by excessive… exertion' and the following symptom description for post-exertional symptom exacerbation which *is* caused by exertion. – Debilitating lack of energy and inability to engage in pre-illness levels of activity might be a preferred first symptom explanation or simply, debilitating exhaustion… etc. – We are not convinced 'fatiguability' in this context is the right fit as the first symptom. – We suggest that to avoid the introduction of new and potentially confusing terms, the breakdown of symptoms and explanations used in the influential Institute of Medicine (now the National Academy of Medicine) 2015 report on ME/CFS is used instead – at least in large part. – We can see no reason why NICE should not take this new guideline as an opportunity to provide a diagnostic criteria that aligns itself with the criteria that has been recognised in America: https://www.cdc.gov/me-cfs/healthcare-providers/diagnosis/iom-2015-diagnostic-criteria.html – Namely: **1.** A substantial reduction or impairment in the ability to engage in pre-illness levels of	Thank you for your comments. *Title* The committee have not edited the title as it is clear in the recommendations that these are the diagnostic criteria for ME/CFS. *Terms used in the guideline* After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms and hope this has added some clarity for readers • *Debilitating fatigability.* This has been edited to be more descriptive of the fatigue experienced by people with ME/CFS, ' 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. Both fatigue and PEM occur after activity and both clarify it is disproportionate to the activity compared to people that do not have ME/CFS. *Order of the symptoms* The symptoms are all required for suspecting ME/CFS and are not in any order of priority.

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				activity (occupational, educational, social, or personal life) that: ▪ lasts for more than 3 months ▪ is accompanied by fatigue/fatiguability that is: • often profound • of new onset (not life-long) • not the result of ongoing or unusual excessive exertion • not substantially alleviated by rest – It is important to stress all of the above points as the first 'symptom' in the diagnostic criteria in the new NICE clinical guideline, although we recognise that the word 'fatigue' is not always relevant or encompassing in this context and the committee might want to substitute this with their preferred term, fatiguability. – Post-exertional symptom exacerbation is another new term that is proposed as a replacement for the current symptom, post-exertional malaise. It is right that this key symptom is included separately and featured prominently (unlike in the current NICE guideline) and we welcome this decision. – But we do not support the introduction of Post-Exertional Symptom Exacerbation (PESE) especially as it is not recognised anywhere else in the literature. We would favour keeping Post-Exertional Malaise (PEM) until such time as the pathology of ME/CFS is better understood. – Again, we refer to the 2015 IOM recommended symptom criteria and recommend this description. – Namely: 2. Post-exertional malaise (PEM) – worsening of symptoms after physical, mental or emotional exertion that would not have caused a problem before the illness:	*Diagnostic criteria* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the Evidence review-D. The committee note the recommendations with the edits address the points you have made about terms used and the descriptions in the terms in the guideline section. To clarify time to diagnosis is still at 3 months, the short time frame to suspecting ME/CFS allows for advice to be given to people before confirming any diagnosis. The committee note that on your last point about 'the diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial, or severe intensity.' Is addressed by the requirement for the symptoms to be persistent.

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				▪ PEM often puts the patient in relapse that may last days, weeks, or even longer. ▪ For some patients, sensory overload (light and sound) can induce PEM. ▪ Symptoms typically get worse 12 to 48 hours after the activity or exposure and can last for days or even weeks. – Unrefreshing Sleep is a recognised symptom and problems with sleep should be a required symptom in this section. However, dysfunctional sleep can mean different things to individuals with ME/CFS and this should also be recognised in any description. – The 2015 IOM description is adequate here but could be expanded to refer to specific issues with sleep. In this instance, the proposed NICE description of Unrefreshing Sleep is preferred. – Namely: 3. Unrefreshing sleep, which may include: ▪ feeling exhausted, flu-like, and stiff on waking. ▪ broken or shallow sleep altered sleep pattern or hypersomnia. – The NICE guideline then proposes Cognitive difficulties are the final main symptom in the diagnostic criteria and we agree with the description. – Whereas the IOM criteria propose a choice between Cognitive Impairment and Orthostatic Intolerance, or the inclusion of both if relevant, we believe it is correct to only include Cognitive Impairment as a required symptom. – Namely: 4. Cognitive difficulties (sometimes described as 'brain fog'), including: ▪ problems finding words, temporary dyslexia, or dyscalculia,	

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				▪ slurred speech, slowed responsiveness, ▪ short-term memory problems, confusion, disorientation, and difficulty concentrating or multitasking. – Orthostatic intolerance may not be a key part of ME/CFS or any disease process and may not apply to everyone with the condition, but it is a commonly reported and often recurring complaint. – Similarly, we feel that 'Flu-like symptoms' in particular should be featured prominently and be a key part of the diagnosis along with 'muscle aches' and 'muscle fatiguability or weakness'. – A final point from the 2015 IOM diagnostic criteria is the inclusion of the following note: 'The diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial, or severe intensity.' We feel that this note should be carried over into the new NICE clinical guideline in respect of the main diagnostic symptoms. ME/CFS is more than the 4 recommended symptoms suggested above, and the new guideline should reflect this fact (see comment 41 below).	
The ME Association	Guideline	001	009	Specifically mention that the guideline is for: Primarily: – General Practitioners, paediatricians, consultants in neurology, immunology etc., hospital-based specialists in ME/CFS, and other healthcare professionals who may come into contact with people who have ME/CFS. – Social care professionals and local authorities involved in providing social care, housing, and social services. – People with symptoms suggestive of ME/CFS and those with a diagnosis of ME/CFS seeking management advice and clinical support, their families, loved ones, carers, and the general public.	Thank you for your comment. It is clear that this guideline applies to all health and social care staff and providers that deliver care to people with ME/CFS and an extended list of professionals or organisations is not necessary. The remit of NICE does not extend to providing guidance for the Department for Work and Pensions (DWP), agencies providing medical assessments for disability benefit purposes, insurance companies, pension providers, employers and education providers but the committee would hope that any organisations who engage with people with ME/CFS would use this guideline as an example of best practice.

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				And also: – Clinical Commissioning Groups (CCGs), hospital trusts and other commissioners of health and social care including local authorities. – The Department for Work and Pensions (DWP) and the agencies providing medical assessments for disability benefit purposes. – Insurance companies and pension providers. Employers and education providers.	The committee consider that, 'people with symptoms suggestive of ME/CFS and those with a diagnosis of ME/CFS seeking management advice and clinical support, their families, loved ones, carers' is covered by 'people with suspected or diagnosed ME/CFS, their families and carers and the public'. The remit of NICE does not extend to the general public.
The ME Association	Guideline	002	003	Covid-19 and clinical vulnerability – Include a note about the possible post-viral fatigue syndrome (PVFS) effects for people who are struggling to recover from Covid-19 infection. – Include that people in this situation could be (and are being) diagnosed with ME/CFS and/or experiencing similar symptoms. – Include that people ME/CFS are clinically vulnerable to Covid-19 infection as this could lead to a significant relapse in their health, and as they are eligible for the free flu vaccine. People with ME/CFS should therefore be eligible for priority treatment with Covid-19 vaccines. – Include that similar management approaches for those with Post-Covid and those with ME/CFS might be applicable e.g., energy management. Refer to the development of a NICE guideline on Post-Covid-19: https://www.nice.org.uk/guidance/indevelopment/gid-ng10179	Thank you for your comment. The guideline was developed before the COVID-19 pandemic and the committee reviewed the evidence relevant to the key areas of the scope. The committee have not reviewed the evidence on COVID-19 and are not in a position to comment or make recommendations in this area either about the long term recovery from COVID-19 or the vulnerability of people with ME/CFS to COVID-19 and prioritisation for vaccines. A link to the now published COVID-19 rapid guideline: managing the long-term effects of COVID-19 has been added.
The ME Association	Guideline	003	002	Improve access to guideline – We would suggest that the new guideline be split into sections to better aid navigation. Namely: 1. Principles of care for people with suspected ME/CFS 2. Principles of care for people with a diagnosis of ME/CFS	Thank you for your comment. Structure After taking into account comments from stakeholders the committee have restructured the guideline and hope that readers will now find it easier to navigate. In particular the special considerations of people with severe and very severe ME/CFS

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				3. Principles of care for people with severe and very severe ME/CFS 4. Principles of care for children and young people with ME/CFS – The draft new guideline is not easy to read or to use to locate specific items relating to the above. – A person needs to read the whole document – and all the links to other NICE guidelines and related information – to appreciate its scope and to find what might be relevant. – We feel that busy health and social care professionals as well as people with ME/CFS who have cognitive challenges would welcome a better presented and more easily navigable document. Introduction – We feel it would be extremely helpful if the new guideline carried an introduction and overview similar in content to the existing guideline: https://www.nice.org.uk/guidance/cg53/resources/chronic-fatigue-syndromemyalgic-encephalomyelitis-or-encephalopathy-diagnosis-and-management-pdf-975505810885 – Please refer to general comments above re: Introduction. Without these key statements it will limit the effectiveness and implementation of the guideline's aims among healthcare professionals and people with ME/CFS.	have been addressed in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline. With reference to children and young people they decide that these recommendations were placed as additional recommendations in the relevant sections. Introduction The structure of NICE guidelines has changed since 2007. The introduction section has been replaced with the context section at the back of the guideline and has updated the information in the 2007 introduction.
The ME Association	Guideline	004	007 - 012	Good description of illness burden but could be more explicit (see comment on Introduction above and suggested Introduction).	Thank you for your comment. This section has been put at the forefront of the guideline to highlight the reality of living with ME/CFS, the rest of the guideline then expands in more detail on how people's lives can be affected and how they can be supported. The introduction section has been replaced with the context section at the back of the guideline and has updated the information in the 2007 introduction.

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The ME Association	Guideline	004	016 - 021	– A welcome section but no advice on how this situation could be resolved. – Express importance of having an assigned health professional in charge of patient's care. – Refer to use of alternative consultation methods that might make a patient feel more comfortable and able to engage with vital healthcare support e.g., telephone and home visits. How can trust be restored? What does the guideline offer to help this situation?	Thank you for your comment. This section has been put at the front of the guideline to highlight the reality of living with ME/CFS, the rest of the guideline then expands in more detail on how people's lives can be affected and how they can be supported. The section on multidisciplinary care recommends a named contact to co-ordinate people's care and support plans. The section on access to care addresses the use of alternative consultation methods. Telephone and home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The committee agree that it is important to restore trust in health and social care services for the people with ME/CFS who have felt let down. Throughout the guideline there is an emphasis on person centered care and shared decision making. This is introduced in a box before the recommendations and then immediately reinforced in the section outlining how care should be delivered. The committee hope these references and those throughout the guideline will reassure people with ME/CFS that they can confidently access health and social care services.
The ME Association	Guideline	004	004 - 006	– Include reference to the items suggested as an introduction above or replace this section with a more complete introduction. – Terminology: Welcome the use of the abbreviation: ME/CFS. – Welcome the use of the term 'medical condition' and the consistency of its use throughout the guideline. Would favour use of 'recognised medical condition' or 'accepted medical condition' in certain instances to help reduce uncertainty, stigma, issues relating to acceptance etc. that people with ME/CFS continue to experience.	Thank you for your comments. Introduction The introduction section has been replaced with the context section at the back of the guideline and includes more detailed information. To note the text 'Myalgic encephalomyelitis is classified under diseases of the nervous system in the SNOMED-CT UK and ICD10 (G93.3)' has been added to the context. The committee agree that it is important to have raise awareness and have clear statements about the reality and seriousness of

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					ME/CFS. The recommendations in the principles for care section do this, the first recommendation states the reality and seriousness of ME/CFS as a medical condition. The addition of 'recognised' or 'accepted' is not necessary. The second recommendation acknowledges that people with ME/CFS have experienced disbelief and stigma. For these reasons your suggestion has not been added.
The ME Association	Guideline	004	013 - 015	– Good description of unpredictability and extent of debilitation (see comment on Introduction above and suggested Introduction). – Suggest remove: 'ranging from being able to carry out most daily activities to severe debilitation,' as this isn't necessary. Recommend that illness severity definitions are included i.e., Mild, Moderate, Severe, and, Very Severe, as this would provide a good overview of the spectrum of ME/CFS.	Thank you for your comment. The committee agreed that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. *Definitions of severity* The committee agreed that the impact of severity exists along a continuum and is not easily categorised. However, to provide an overview of the spectrum of ME/CFS definitions of severity have been included in the guideline.
The ME Association	Guideline	004	002 - 003	It would be helpful if it was made clear who this section is for exactly.	Thank you for your comment. This section aims to raise awareness of ME/CFS and is directed at readers the guideline.
The ME Association	Guideline	004	001	– Prescribing medicines – there are some helpful medications which should be considered for several symptoms like pain and sleep.	Thank you for your comment. Although pain relief and sleep medication was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make

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				– See recommendation below for chapter on Symptom Management. – The guideline should clearly state that GPs etc. should consider symptom-relieving medications and alternative treatment options for people with ME/CFS. – We are acutely aware that while some people with ME/CFS are benefitting from symptom-relieving medications, others are not. We need to ensure that all options are considered for all people with the condition and specifically mentioning it here in the guideline will help.	any recommendations for specific medications. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. . The committee have also added consensus recommendations on sleep with referral to a specialist if appropriate. As you note Medicines for symptom management is included in the symptom management section of the guideline and medicines management is listed as expertise needed by people with ME/CFS indicating the importance of considering this for people with ME/CFS. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made and then reinforced in the management section of the guideline and for this reason your suggestion has not been added to the recommendation.
The ME Association	Guideline	005	002 - 008	– It would be helpful to refer to specific health professionals in charge of a person's care e.g., General Practitioners, ME/CFS specialists, paediatricians and other clinical consultants, social care professionals etc. – Inform the person that ME/CFS is an accepted medical condition and acknowledge the difficulties that arise from living with ME/CFS. – Provide information on the possible causes, nature, and likely course of the disease – refer to suggested introduction and content in comment above.	Thank you for your comment. The points you suggested are addressed in other areas of the guideline; multidisciplinary care, information and support and access to care. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.

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				– Take account the person's age (particularly children younger than 12 years), the severity of ME/CFS, the degree of disability, whether home support is available, preferences and experiences, and any co-morbid medical conditions. Healthcare professionals should be aware that cognitive symptoms may mean that the person with ME/CFS has problems communicating and retaining verbal information.	The committee note that the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse
The ME Association	Guideline	005	20-26	There is no suggestion as to how to deal with these occurrences or who might be responsible for helping parents and children best manage the situation to achieve a satisfactory resolution.	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience. The current wording addresses this. The committee did not review the evidence on how a breakdown of a therapeutic relationship this could be addressed and are unable to make any recommendation on this. Although it is hoped that following the recommendations in this guideline this could be avoided.
The ME Association	Guideline	005	015 - 018	Consider replacing 'management plan' with 'care plan' and stress that withdrawal should not mean that people with ME/CFS are left without the care and support of a nominated GP, specialist, paediatrician, other health, or social care professional, or excluded from regular reviews and follow-ups e.g., continuity of care remains a priority particularly for the severely/very severely affected, children and young people.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The ME Association	Guideline	005	012 - 014	Include: regular monitoring and review from the appointed health and/or social care professional, particularly when symptoms are worsening or new symptoms occur, that includes updating the personalised care plan (see section of managing flares and relapses).	Thank you for your comment. This recommendation is to raises awareness about the importance of review and monitoring for people with ME/CFS. The review in primary care section of the guideline has further detail on reviews and who should do this and this link has been added here. For this reason your suggestion has not been added.

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The ME Association	Guideline	005	010 - 011	Include: early and accurate diagnosis from the appointed healthcare professional so people receive timely and accurate medical advice relating to care and symptom management including a personalised care plan.	Thank you for your comment. This recommendation is to raises awareness about the importance of a timely and accurate diagnosis for people with ME/CFS. The following suspecting ME/CFS, advice for people with suspected ME/CFS and diagnosis sections have further detail on the points you make. For this reason your suggestion has not been added.
The ME Association	Guideline	006	007	– Suggest sub-title is changed to be more in-line with previous section i.e.: 1.1.8 Additional principals of care for people severely or very severely affected by ME/CFS – Suggest a new opening paragraph is included that highlights the need for greater health and social care involvement and refers to the possible extent of disability. – For example, those severely affected will be housebound or bedbound, those very severely affected will be bedbound and are likely to require 24-hour care etc. Health and social care professionals should be left in no doubt as to the extent of the care that might be required when helping people in this situation or of the importance of being directly involved.	Thank you for your comment. Taking into account the range of stakeholder comments on the descriptions of severity in the guideline the committee have moved the recommendations on people with severe and very severe ME/CFS into a separate section to ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. This section includes recommendations on support and access to care.
The ME Association	Guideline	006	022	– We welcome the mentioned of gastrointestinal difficulties or symptoms, but this is not limited to those severely affected as GI symptoms are widespread features for less severely affected as well. Gastrointestinal difficulties are more commonly referred to as functional gut symptoms, IBS (Irritable bowel Syndrome)-type symptoms, or gastrointestinal symptoms.	Thank you for your comments. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline but would also clarify that symptoms in the section suspecting ME/CFS can be experienced by all people with ME/CFS.

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					To note that gastrointestinal symptoms has been added to the symptoms that may be associated with ME/CFS in the section on suspecting ME/CFS and the IBS guideline added to the list of guidelines in the coexisting conditions section of the guideline.
The ME Association	Guideline	007	017 - 021	– Suggest including specific reference to the healthcare professional who is responsible for the care of the person severely or very severely affected e.g., General Practitioner, Paediatrician, ME/CFS specialist, social care professional etc. Recommend that the person responsible is clinically aware of – and has personal experience of – ME/CFS and recognises that they could be caring for someone who may be wholly reliant on the support of others i.e. is potentially in a dire situation.	Thank you for your comment. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
The ME Association	Guideline	007	008 - 010	Include: May not be able to communicate effectively or at all without support and may need someone else to communicate on their behalf.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The ME Association	Guideline	007	011 - 013	Include reference to risk of malnutrition especially for those very severely affected and possible use of feeding tubes etc.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The ME Association	Guideline	007	014 - 016	This is applicable to difficulties relating to effective communication and should include use of telephone and length of time spent interacting with others etc.	Thank you for your comment. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The ME Association	Guideline	007	004 - 005	– Include: are housebound or bedbound and may need support with all activities of daily living.	Thank you for your comment. The level of support needed is individual to the person and agreed as part of their personalised care and support plan. As

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				People very severely affected are likely to require 24-hour care and support from health and social care professionals and family members.	such it is not always appropriate to put in details about levels of care and for this reason your suggestion has not been added.
The ME Association	Guideline	007	022 - 016	– Due consideration must be given to the effects of not providing care and support to people in these situations. – Monitoring and reviewing progress, providing suitable care measures and disability aids and appliances, ensuring prescriptions are suitable, that drips, catheters, nutritional systems etc. are reviewed and replaced, that a person is being visited by health and social care professionals regularly – even if only to speak with the patient's family – is essential. Risk assessments should not result in a loss of care or leave the patient or their family without support or a medical and social care professional with whom they can refer in an emergency.	Thank you for your comment. The committee agree that people with severe or very severe ME/CFS require care to support them and this is reinforced throughout the guideline addressing the areas of care you raise. The committee note that level and type of support needed is individual to the person and agreed as part of their personalised care and support plan. This would include assessing the risks of interactions and ensure people with severe or very severe ME/CFS receive care that is appropriate to their needs.
The ME Association	Guideline	007	008	Include: Will require use of disability aids and adaptations to assist with daily living and/or to help mobilise e.g., wheelchair, walker, mobility scooter etc.	Thank you for your comment. After considering the range of stakeholder comments this has been edited to, 'are housebound or bed-bound and may need support with all activities of daily living, including aids and adaptions to assist mobility and independence in activities of daily living (for example wheelchairs)' The section on aids and adaptions provides further information. These are examples in the recommendations and as with any list of examples these cannot be exhaustive for this reason your suggestions have not been added.
The ME Association	Guideline	008	010 - 016	– Suggest the order of these points is rearranged. The significant loss of ability to engage in pre-illness activities resulting in sickness absences from employment or education is often the main reason for involving a healthcare professional in the beginning. Suggest including reference to likely triggering events e.g., recent viral or bacterial infection the symptoms of which and	Thank you for your comment. The points are all required for suspecting ME/CFS and are not in any order of priority. The committee discussed the inclusion of triggering events but decided not to include reference to this as it is not clear what causes ME/CFS and the inclusion of any examples of triggers may be taken as an absolute list. The context section notes that

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				inability to return to pre-illness levels of health are key reasons for referral to a person's GP or other healthcare professional.	in many cases, symptoms are thought to be triggered by an infection.
The ME Association	Guideline	008	001 - 004	– Recommend that the first action a General Practitioner, specialist, consultant, or paediatrician does is to acknowledge the reality of ME/CFS (refer to 1.1.3 and reiterate these principals before explaining there is no diagnostic test at present). Consider using an amended version of the paragraph from the current guideline (1.2.11) for example: 'ME/CFS is suspected and diagnosed based on clinical assessment and exclusionary testing. It is an accepted and valid medical condition despite the lack of a specific diagnostic test at this time. Primary healthcare professionals should be familiar with and be able to identify the characteristic features ME/CFS and, once a diagnosis has been made, healthcare professionals and patients should feel confident about it.'	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As you note this point is made earlier and this principle is reinforced throughout the guideline and for this reason your suggestion has not been added to the recommendation. The committee agreed that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
The ME Association	Guideline	008	005 - 008	There should be some attempt at standardising clinical assessments and providing health professionals with more guidance in this regard.	Thank you for your comment. The terms used in the guideline define further fatigue, post exertional malaise and unrefreshing sleep. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. The committee note that the assessment recommended describes the routine examinations and assessments when a patient has an undiagnosed illness.
The ME Association	Guideline	008	011 - 012	It may not have been possible for patients to have consulted their primary care physician during acute phase of illness and this should be acknowledged.	Thank you for your comment. In the access to care section of the guideline there is a recommendation that raises awareness that people with ME/CFS are unlikely to be seen at their worst.

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The ME Association	Guideline	008	009	– Baseline investigations to exclude other diagnoses: These investigations should be clearly defined (see below) and NICE should include an approved list of baseline investigations and not leave this solely to clinical opinion. – People with ME/CFS need to receive a standard set of e.g., exclusionary blood tests at the time ME/CFS is suspected and at other times when new or worsening symptoms cause concern and/or a marked deterioration in health. – See current NICE guideline 1.2.2 and 1.2.2.3 in particular for a list of exclusionary blood tests. Exclusionary diagnoses and comorbidities – We also feel that advice should be given on exclusionary diagnoses that might account for symptoms and for other conditions that might have been diagnosed previously or occur subsequently. – We would also like to see included the 'red flags' referred to in the current guideline at 1.2.1.4. – Common exclusionary and comorbid diagnoses should be provided as examples. – Health professionals should be advised that certain other diagnoses do not necessarily prevent a diagnosis of ME/CFS, for example: • Fibromyalgia (FM) should be included as a potential comorbidity and as an alternative explanation if joint and skeletal pain (not muscular aches and pains) are primary symptoms and the test for FM is positive. • Irritable Bowel Syndrome (IBS) is another potential co-morbidity although IBS-like symptoms are also commonly reported as part of ME/CFS. • Anxiety and depression which can be a result of having ME/CFS and trying to live with a chronic condition might also form part of a differential diagnosis.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations. *Exclusionary diagnoses and comorbidities* The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. The discussion section of Evidence review D- Diagnosis includes a list of differential diagnosis and conditions that commonly occur in people with ME/CFS and has the examples you have listed.

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				• Vitamin D and other vitamin/mineral deficiencies should be included on the list of alternate things to consider as potentially contributing or causing symptoms... – Psychological and/or psychiatric conditions can also be differential diagnoses and might exclude a diagnosis of ME/CFS along with other diagnoses that can be shown to explain symptoms and the degree of disability being experienced. Include note that this guideline does not include advice on management of differential diagnoses and refer to other relevant guidelines etc.	
The ME Association	Guideline	008	014	Include reference to likely sickness absences from employment or education and that symptoms can cause significant 'functional incapacity' affecting all aspects of a person's life.	Thank you for your comment. The committee consider that wording of this bullet point in the recommendation, 'if ….the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' covers the aspects you raise and would not any further clarity. For this reason your suggestion has not been added.
The ME Association	Guideline	008	016	– Symptoms may not be new, but they are likely to have had a specific onset in most instances; although this may not be apparent to all it should be discussed and agreed with a person's primary care physician. – Symptoms could be familiar if e.g., a person has been incapacitated due to a recent viral or bacterial infection that might have passed but left them with a post-viral fatigue syndrome (PVFS). In this example, symptoms are likely to have persisted and a diagnosis of ME/CFS may become appropriate if they have continued and resulted in significant incapacity compared to pre-illness levels of function, for 3 months in adults and children (1.4.1).	Thank you for your comment. After considering the stakeholder comments this bullet point has been deleted. On reflection the bullet point above in recommendation 1.2.4,' the person's ability to engage in occupational, educational, social or personal activities is significantly reduced from pre-illness levels' indicates that the symptoms have developed and have not always been present covering that the symptoms are not lifelong.
The ME Association	Guideline	009	001 - 016	One or more of the following symptoms… – Continued from comment above.	Thank you for your comment.

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				– We would refer the committee to the way in which the current guideline (1.2.1.2) states: 'one of more of the following symptoms' and then lists the symptoms commonly reported to be part of ME/CFS in addition to the 4 main symptom requirements. – In the new guideline the list of associated symptoms do not form part of the diagnostic criteria and we feel strongly that they should. – Health professionals should be left in no doubt that a diagnosis can only be made if the 4 key symptoms are present *and* at least one or more of the associated symptoms i.e., a diagnosis should not be made without them. – We have rearranged the list of additional symptoms in order of what we believe is the more important. – Namely we would suggest: 5. At least one or more of the following symptoms: ▪ flu-like symptoms, including sore throat, tender glands, nausea, chills, and/or muscle aches. ▪ orthostatic intolerance and autonomic dysfunction, including dizziness, vertigo, palpitations, fainting, nausea on standing or sitting upright from a reclining position. ▪ pain, including pain on touch, myalgia, headaches, eye pain, abdominal pain, or joint pain without acute redness, swelling or effusion. ▪ heightened sensory sensitivities, including to light, noise, touch, smell, and taste. ▪ temperature hypersensitivity resulting in profuse sweating, chills, hot flushes, or feeling very cold.	In the committee discussion section in Evidence review D the committee reason that while these criteria are commonly experienced by people with ME/CFS they are not key to the diagnosis and their inclusion as criterion is not supported by the evidence or the committee's experience. In addition, the inclusion of at least one of these associated symptoms as a key criterion would not add any clarity to the criteria and would potentially add confusion. This addition could potentially mean that some people with ME/CFS would not be diagnosed or get a delayed diagnosis. For these reasons the committee have not included your suggestion. The committee discussed the other symptoms you suggested should be on the list and they agreed to add gastrointestinal symptoms to the list and taste has been added to the list of heightened sensitivities. Based on the evidence reviewed in evidence review D and on their experience the committee did not agree that urinary symptoms, weight loss or visual disturbances should be included in the list of associated symptoms. The committee note that urinary symptoms are listed in the examples of differential diagnosis in evidence review D and appetite, weight gain and visual disturbances are highlighted in recommendations within the guideline with reference to the description of or the management of symptoms. This is the criteria for suspecting ME/CFS, frequency and severity is not relevant but as you note further detail is given about the fluctuating nature of ME/CFS and the range of severity in other sections of the guideline.

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				▪ neuromuscular symptoms, including twitching and myoclonic jerks. ▪ intolerance to alcohol, or to certain foods, and chemicals. – We would also like to see included in the list above, the following symptoms: • irritable bowel syndrome (IBS), or IBS-type symptoms, frequent episodes of diarrhoea and bowel discomfort. • urinary incontinence and/or an increase in urinary frequency etc. • weight loss or gain and changes in appetite and nutritional intake ability. • visual disturbances that can prevent or limit visual capacity and reading ability. – Please note the addition of 'taste' to the list of sensory sensitivities above. In our experience this can present with specific new texture aversions. These can be very pronounced in the most severely affected, impacting adversely nutritional intake and significantly limiting the variety of foods eaten. – Symptoms are especially acute in the early stages of ME/CFS and/or when the condition is at its worst during periods of post-exertional malaise or relapse or when people are severely or very severely affected. This should be recognised in this section about diagnosis. Frequency of symptoms and symptom severity should also be mentioned in this section alongside the often-fluctuating nature of symptom intensity and duration (see current guideline 1.2.1.3.).	
The ME Association	Guideline	009	017 - 020	– Provisional diagnosis should not be delayed, based on criteria *and* comprehensive clinical examination and assessment etc. We would also like to see reference made to the consideration of prescription medications to help relieve symptoms as well as	Thank you for your comment. Based on the qualitative evidence and their experience the committee agree it is important that people with this combination

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				advice on symptom management and implementation of a mutually agreed care plan and regular reviews.	of symptoms are given advice that may prevent them getting worse as early as possible. After considering the range of stakeholder comments on the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS. In summary the edits are: ○ The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. ○ The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis. These edits do not change the recommendations that people with suspected ME/CFS should be given advice in section 1.3. In section 1.3 the first recommendation starts with 'give people personalised advice about managing their symptoms' appropriate prescription medicines would be more specific to the individual and included here. As with all examples in recommendations they are not intended to be exhaustive.
The ME Association	Guideline	009	021 - 023	This continuity of care and support should be a theme throughout the new guideline. People with suspected ME/CFS or those with a diagnosis should not feel abandoned or left to cope alone.	Thank you for your comment. The committee agree and continuity of care is a theme throughout the guideline. In particular see the section on multidisciplinary care.
The ME Association	Guideline	010	017 - 021	Examples welcome but would like to see the consideration of use of appropriate prescription medications to help symptom relief and of other approaches e.g., OTC medications etc.	Thank you for your comment. This recommendation starts with 'give people personalised advice about managing their symptoms' appropriate prescription medicines would be more specific to the individual and included

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					here. As with all examples in recommendations they are not intended to be exhaustive.
The ME Association	Guideline	010	001 - 003	Would favour some key examples of the type of specialist likely to be involved in exclusionary considerations and in making a formal diagnosis of ME/CFS. For example, General Practitioners, Paediatricians, referral to ME/CFS specialist physicians, neurologists, immunologists, rheumatologists, etc.	Thank you for your comment. The committee discussed the addition of examples of specialists but came to the conclusion that any list could not be exhaustive and there is the risk that the examples given are seen as the only specialists to refer to. For this reason the committee did not add your suggestion.
The ME Association	Guideline	010	004 - 006	– Would be helpful to specifically mention that any suspicion is likely to come from the General Practitioner. GPs should be clearly aware of their roles and responsibilities throughout the guideline – along with other professionals likely to be involved in the care of people with ME/CFS.	Thank you for your comment. The committee agree that it is likely that it will primary care that will be suspecting ME/CFS and making a referral for confirmation of the diagnosis but it could also be other clinicians people are receiving care from. For this reason the committee did not add your suggestion. The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline.
The ME Association	Guideline	011	009 - 012	– ME/CFS specialist services are not available in all areas and the guideline should reflect this fact. Paediatricians should be named as primary providers and the main points of contact. – A care plan should be something primary physicians are responsible for creating and reviewing regularly and a care plan should include the ME/CFS management plan. The management plan should be something a Paediatrician is capable of creating when a specialist service is not available. The Paediatrician can personalise and agree it with the patient and be responsible for reviewing progress etc. during subsequent consultations.	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres

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					A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The ME Association	Guideline	011	015 - 018	– See comment (50) above. – It would be useful to see a note that assessments, care, and management plans can be produced and discussed either in person, or by alternative means depending on the ability of the person with ME/CFS. – For those housebound or bedbound then assessments and ongoing reviews by telephone or video conference might be more conducive than in-person consultations. – If a person is severely or very severely affected, then home visits might be a more suitable alternative but the person with ME/CFS or a nominated representative should be able to choose. We would appreciate a specific reference to consideration of symptom relieving medications. This decision should not be left solely to a GPs or specialist's opinion but should form a key part of any holistic assessment and ongoing care and management plan.	Thank you for your comment. *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The recommendations on developing the care and support plan now include a reference to the medicines management section in the symptom management section.
The ME Association	Guideline	011	004 - 006	– Include 'at least 3 months'? – Include the following statement (see current guideline 1.3.1.3) (edited):	Thank you for your comment. After considering stakeholder comments about the a provisional diagnosis, this has been edited to ensure that before 3 months ME/CFS is suspected not diagnosed, it is now clearer that

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				'The diagnosis of ME/CFS should be reconsidered if none of the following key features are present: 1. A substantial reduction or impairment in the ability to engage in pre-illness levels of activity… 2. Post-exertional malaise… 3. Unrefreshing sleep… Cognitive difficulties…	diagnosis happens when symptoms have been present for 3 months and is then confirmed by a ME/CS specialist team. Adding at least 3 months does not add any further clarity, if symptoms have been present for more than 3 months this recommendation still applies. Recommendation 1.4.1 refers back to the key criteria and is clear that these symptoms all have to be present for a diagnosis. A recommendation has been added to this section reinforcing the importance of seeking advice if there is uncertainty about interpreting signs and symptoms. For these reasons your suggestions have not been added.
The ME Association	Guideline	011	001 - 002	– Responsibility for this aspect of the guideline should clearly lie with General Practitioners and medical professionals involved in specialist care, paediatricians etc. – Welcome reference to continuing care but the GP and/or specialist should be the named point of contact for any further complications. – When does the 3-month diagnostic deadline commence? From the point a person first meets with their GP and reports symptoms or when symptoms actually began? If someone has had symptoms for some time it might not have been possible to meet with their GP or they might only seek help and support when symptoms permit, or a person is in considerable distress.	Thank you for your comment. The committee agree that this is likely to be the person's GP but this might not always be the case and the committee have in the recommendation people should be told who they can contact for advice. Recommendation 1.4.1 is clear that diagnosis occurs when symptoms have persisted for 3 months.
The ME Association	Guideline	011	007 - 008	– ME/CFS specialist services are not available in all areas and the guideline should reflect this fact. GPs should be named as primary providers and the main points of contact. – A care plan should be something primary physicians are responsible for creating and reviewing regularly and a care plan should include the ME/CFS management plan. The management plan should be something a GP etc. is capable of creating when a specialist service is not available. The GP can	Thank you for your comment. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I-Multidisciplinary care, they note that in particular children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS

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				personalise and agree it with the patient and be responsible for reviewing progress etc. during subsequent consultations.	specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres. A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. Based on the evidence (see evidence report I) and in the committee's experience clinicians working within a ME/CFS specialist team are the best healthcare professionals to develop a care and support plan, they have the expertise in ME/CFS and the understanding of the detailed assessment required at this stage. For this reason the committee have recommended that diagnosis and the development of the care and support plan should be carried out by a ME/CFS specialist team. Any clinician not working in collaboration with and supported by a ME/CFS specialist team should not be developing the care and support plan. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The ME Association	Guideline	011	013 - 014	– A specialist ME/CFS team are the ideal but primary healthcare professionals should also be capable of producing an assessment and reviewing a care and management plan. – An explanation of what a specialist team might comprise would be welcome here. Not all areas in England are covered by ME/CFS specialist support and those services that do exist can vary in composition. – It might help if NICE were to explain the kind of support specialist services should be providing, e.g., as a minimum –	Thank you for your comment. Based on the evidence and in the committee's experience clinicians working within a ME/CFS specialist team are the best healthcare professionals to develop a care and support plan, they have the expertise in ME/CFS and the understanding of the detailed assessment required at this stage. For this reason the committee have recommended that diagnosis and the development of the care and support plan should be carried out by a ME/CFS specialist team. Any clinician not working in collaboration with and supported by a ME/CFS specialist team should not be developing the care and support plan. The

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				second opinions re: diagnosis, actual diagnosis, ongoing care, and management support. – It should be mentioned that anyone with ME/CFS can ask for a referral to a specialist service even if they need to do so out of their area because of a lack of availability. However, attendance is largely based on the patient being ambulatory. – It should be mentioned that GPs and specialist services are able to provide home visits to those severely or very severely affected. – Joint decision making should also be referred to and that care and management plans should be personalised and relevant to the individual. We would appreciate a specific reference to consideration of symptom relieving medications. This decision should not be left solely to a GPs or specialist's opinion but should form a key part of any holistic assessment and ongoing care and management plan.	committee agree that review of the care and support plan can take place in primary care and this is set out in the review in primary care section of the guideline. The committee agree there is inequity in the provision of services and access to ME/CFS specialist teams. They discuss further access to ME/CFS specialist teams in Evidence review I- Multidisciplinary care, they note that children and young people are likely to be cared for under local or regional paediatric teams that have experience working with children and young people with ME/CFS in collaboration with ME/CFS specialist centres. In these situations confirmation of diagnosis and the development of the care and support plan is supported by the ME/CFS specialist centres A description of ME/CFS specialist teams has been added to the terms used in the guideline and this includes the model with local and regional teams. Throughout the guideline where it is relevant that specific expertise from a ME/CFS specialist team is needed this is recommended. For example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. Access to services The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access

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					care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. Joint decision making The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) The recommendations on developing the care and support plan now include a reference to the medicines management section in the symptom management section.
The ME Association	Guideline	012	010 - 030	Include specific reference to consideration of suitable symptom-relieving medications and a note that while we wait for an effective treatment to be discovered, the illness can be managed in most cases with help from nominated healthcare professionals and ME/CFS specialists.	Thank you for your comment. 'Including medicines management ' has been added to the symptom management bullet point . The symptom management section includes recommendations on medicines management.
The ME Association	Guideline	012	7-9	Dietary assessment should include assessment of diet, food, or gut-related symptoms in order to pave the way for this to be included in the management section.	Thank you for your comment. The list of examples was identified by the committee based on their experience of what can be included in an assessment but is not intended to be an exhaustive list.

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The ME Association	Guideline	012	004	psychosocial wellbeing should be defined to include the impact of ME/CFS on mental health as a consequence of having to cope, accept and adapt to symptoms and any resulting disability and problems with income security, housing, employment, social activities, relationships and lifestyle etc.	Thank you for your comment. After considering the range of stakeholder comments, this bullet point has been edited to, 'the impact of symptoms on psychological, emotional and social wellbeing'.
The ME Association	Guideline	013	001 - 008	Would like to see included that the person with ME/CFS or their representative can withdraw from any element of care or the management plan etc. when they choose to do so and without it effecting the continuity of care received from the GP or specialist service etc.	Thank you for your comment. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is addressed in the principles of care section of the guideline and for this reason your suggestion has not been added to the recommendation.
The ME Association	Guideline	013	011 - 013	– It would be helpful if the guideline mentioned who should be responsible for home visits e.g., General Practitioner, ME/CFS specialist, Paediatrician etc. – It is essential that people who are most vulnerable are not left to fend for themselves, and that all efforts are made to help support their needs and make them comfortable. – Home visits can and should be supplemented with telephone and/or video consultations, and a named healthcare professional should be available for any additional problems the person with ME/CFS or their representative might encounter. Home visits and alternate means of contact should not be limited to holistic assessments and discussions of any care of management plan. They are an often-essential means of medical and social care intervention.	Thank you for your comment. This recommendation refers to the holistic assessment and care and support plan and this is developed by the ME/CFS specialist care team. The committee note that the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse *Access to care* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. In the access to care section and in the section for people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access

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					care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. .
The ME Association	Guideline	013	009 - 010	– There should be a direct two-way line of communication between ME/CFS specialist services and a person's GP or Paediatrician and medical notes should carry up to date copies of the care and management plan etc. – The person with ME/CFS or their representative should be involved in all communications and be party to all decisions made in relation to their care. The person with ME/CFS should feel they are supported by the NHS and listened to and not left to fend for themselves.	Thank you for your comment. The committee agree that collaboration is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. To note management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)
The ME Association	Guideline	013	014	Would be helpful to specify the healthcare professionals who are responsible for maintaining effective communication with people who have ME/CFS.	Thank you for your comment. In the Multidisciplinary care section of the guideline the committee have recommended that people with ME/CFS are given a named contact.
The ME Association	Guideline	014	015 -031	– Would like to see inclusion of symptom-relieving prescription medication as part of ongoing management. – Self-management is not the only option for people with ME/CFS and GPs and specialists can help by recommending appropriate use of medications to help with pain and sleep for example.	Thank you for your comment. *Medicines* Although pain relief and sleep medication were explicitly included in the protocol for pharmacological interventions no evidence

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				Include reference to the 2010 Equality Act where ME/CFS is recognised as a qualifying disability: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/570382/Equality_Act_2010-disability_definition.pdf	was identified and the committee agreed they were unable to make any recommendations for specific medications. *Pain* The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate. *Sleep* After taking into consideration the stakeholders comments the committee have added general advice on sleep management. *Equality Act 2010* In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS.
The ME Association	Guideline	014	008 - 014	– Include reference to information about comorbidities where applicable – a holistic approach – and specify what form this information is to be in and who might produce it. It is a good principle to have but who is to produce the information and maintain it or is the information being referred to solely that contained in the NICE clinical guideline?	Thank you for your comment. This recommendation is about information about ME/CFS, if information on comorbidities is appropriate then this would be a decision between the person and the health care professional. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering

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					care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. . See evidence review B – information for health and social care professionals for the evidence and committee discussion on this topic.
The ME Association	Guideline	015	011 - 015	– Recommend a definition of social care be included within this section as it is not commonly known what it might comprise or how useful it could be. – 'Sensitively discuss' – 'care needs assessment' Insert link to section 1.8.7 Maintaining independence which explains what is required for a social care needs assessment.	Thank you for your comment. The first recommendation in this section refers to the NICE guideline on people's experience in adult social care services and provides detailed information on social care. A link to the section on maintaining independence has been added. The committee agreed that your other points did not add further clarity to the recommendation and these have not been added.
The ME Association	Guideline	015	004 - 007	Include recognised ME/CFS charities like The ME Association who operate nationally.	Thank you for your comment. The committee agreed not to add examples of organisations, as with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.
The ME Association	Guideline	015	019 - 022	– It would be helpful if the healthcare professional with this responsibility and ability to be involved children's social care could be mentioned specifically. Include reference to the 2014 Care Act and link to the helpful NHS Choices social care guide: https://www.nhs.uk/conditions/social-care-and-support-guide/	Thank you for your comment. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, and to help them access services. The first recommendation in this section refers to the NICE guideline on people's experience in adult social care services and provides detailed information on social care and references the 2014 Care Act. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much

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					repetition results in a guideline becoming unwieldy and unusable. This point is made in the guideline and for this reason your suggestion has not been added to the recommendation
The ME Association	Guideline	015	001 - 003	– We would like to see more information about prevalence, prognosis, permanency, disability, and quality of life for people with ME/CFS. This could be discussed in an Introduction at the start of the guideline. It is an area that everyone with ME/CFS is concerned about and it should be given greater prominence in the clinical guideline, perhaps even having its own section.	Thank you for your comment. This information is given in recommendation 1.6.4 in the information and support section.
The ME Association	Guideline	015	016 - 018	– It is important here to specifically mention the healthcare professional that can make an application for a care needs assessment and liaise with the local authority. – Not all people with ME/CFS have family support and the help from a suitable healthcare professional in this instance will be especially necessary. Include reference to the 2014 Care Act and link to the helpful NHS Choices social care guide: https://www.nhs.uk/conditions/social-care-and-support-guide/	Thank you for your comment. The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, and to help them access services. The first recommendation in this section refers to the NICE guideline on people's experience in adult social care services and provides detailed information on social care and references the 2014 Care Act. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. This point is made in the guideline and for this reason your suggestion has not been added to the recommendation
The ME Association	Guideline	015	024 - 026	It would be helpful to mention the main benefits that are available to carers of people with ME/CFS e.g., Carers Allowance.	Thank you for your comment. The sub section on supporting families and carers of people with ME/CFS includes reference to the NICE guideline on supporting carers and this has more detailed information.
The ME Association	Guideline	015	009 -010	– It would help if NICE were clearer about the origin of this information and who is responsible for maintaining it.	Thank you for your comment. This recommendation is an action for health and social care professionals. The committee agree that training for health and

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				Is NICE referring to standardised information based on the guideline and produced by NICE or some other form of written etc. information about ME/CFS that is being produced and will be maintained?	social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
The ME Association	Guideline	015	008	– This has proven to be an issue for people with ME/CFS and should be a key point in the guideline – not a secondary bullet point. – It would be helpful here if NICE were clear about which healthcare professional is responsible for providing free medical reports and help supporting benefit applications and subsequent reviews by the Department for Work and Pensions or its agencies. – We need to feel confident that the NHS is able to provide suitable and accurate reports and that people with ME/CFS are able to draw on this vital support as and when necessary. – Include reference to the 2010 Equality Act where ME/CFS is recognised as a qualifying disability: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/570382/Equality_Act_2010-disability_definition.pdf Include reference to the main disability benefits: Employment and Support Allowance, Universal Credit, and, Personal Independence Payment.	Thank you for your comment. The committee note the bullet points are not in order of priority. It is not within NICE'S remit to make recommendations about which healthcare professional is responsible for providing free medical reports and help supporting benefit applications and subsequent reviews by the Department for Work and Pensions or its agencies. *Equality Act 2010* In the supporting people with ME/CFS in work, education and training section of the guideline there is direct reference to the Equality Act 2010 and how it could support people with ME/CFS. The section on social care provides further information on accessing support.
The ME Association	Guideline	016	005 - 015	– We very much welcome these sections on safeguarding principles for adults. – It would be helpful if the healthcare professionals most likely to be involved in safeguarding were mentioned by role e.g., General Practitioners, ME/CFS specialists, paediatricians. – Any of the above-mentioned healthcare professionals should have experience in ME/CFS but safeguarding should not be	Thank you for your comment. Health and social care professionals includes the examples you have given and the committee agreed not to add examples of professionals, as with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available.

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				limited to those with such experience as the principles are applicable to anyone involved in the care and support of people with ME/CFS. Appropriate action and support should not be delayed because of a lack of experience in ME/CFS.	The committee agree and recommend in the training for health and social care professionals section of the guideline that all staff that deliver care to people with ME/CFS should maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline.
The ME Association	Guideline	017	008 - 019	This section is particularly welcome and should be applicable to professionals involved in the delivery of health and social care in particular but also to ME/CFS specialists.	Thank you for your comment.
The ME Association	Guideline	017	001 - 007	– We very much welcome these sections on safeguarding principle for children and young people. – It would be helpful if the healthcare professionals most likely to be involved in safeguarding were mentioned by role e.g., General Practitioners, ME/CFS specialists, paediatricians. – Any of the above-mentioned healthcare professionals should have experience in ME/CFS but safeguarding should not be limited to those with such experience as the principles are applicable to anyone involved in the care and support of people with ME/CFS. Appropriate action and support should not be delayed because of a lack of experience in ME/CFS.	Thank you for your comment. Health and social care professionals includes the examples you have given and the committee agreed not to add examples of professionals, as with any list of examples these cannot be exhaustive and there is the risk these are taken as the only options available. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
The ME Association	Guideline	018	001 - 009	'Service providers' should be better defined and include health and social care professionals, ME/CFS specialists, Department of Work and Pensions assessors etc.	Thank you for your comment. This has been edited to,' health and social care organisations' to clarify it is the responsibly of the trusts and organisations to enable health and social care professional to implement this recommendation. The remit of NICE does not extend to providing guidance for the Department for Work and Pensions (DWP) but the committee would hope that any organisations who engage with people with ME/CFS would use this guideline as an example of best practice.

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The ME Association	Guideline	018	013 - 018	– Add that people severely or very severely affected may not be seen because of the severity of their symptoms and difficulties communicating or because of extreme sensitivity to light, noise, touch etc. – It may only be possible to speak with a family member, carer, or representative of the person with ME/CFS, but this should not prevent or postpone health and social care interventions, reviews, or assessments. Adaptations to the normal way in which health and social care professionals provide care and support will need to be employed in such instances.	Thank you for your comment. This information is included in the section on people with severe and very severe ME/CFS and is highlighted in the awareness of severe and very severe ME/CFS and its impact section. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. and for this reason your suggestion has not been added to the recommendation.
The ME Association	Guideline	018	019 - 024	A proactive and flexible approach should also be offered to others who are housebound or bedbound i.e., moderately affected or when people are experiencing poor periods of health e.g., relapse or post-exertional malaise or because of other reasons e.g., infections that might have triggered worse health.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
The ME Association	Guideline	018	010 - 012	– People with ME/CFS are discharged from health and specialist care because of their inability to attend appointments when health has deteriorated or because it is wrongly felt that nothing can be done to support them. – Continuity of care is vital, and a nominated healthcare professional should take responsibility for ensuring care is provided and follow-ups made when contact has been lost in such circumstances. No person with ME/CFS should feel isolated from the NHS because this cab compound the distress they feel and may lead to health complications that could be avoided by regular and helpful interventions.	Thank you for your comment. Discharge The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support. Named contact

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					The multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. Access to services The committee agree that no one should feel isolated from the NHS and that flexibility in accessing services is important to all people with ME/CFS. They recognise that the symptoms experienced can mean physically attending appointments can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
The ME Association	Guideline	018	013 - 014	While awareness of these explanations is important, it would be helpful if the guideline explained what action should occur in these circumstances.	Thank you for your comment. This recommendation raises awareness why people with ME/CFS may have difficulty accessing services and the implications of this. This section recommends how people with ME/CFS could be supported at times when accessing services is particularly difficult for them.
The ME Association	Guideline	018	015 - 016	– Remove the word, 'fear'. Relapse and post-exertional malaise or because people with ME/CFS are enduring a period of poorer health, or are moderately, severely, or very severely affected and unable to mobilise effectively, are reasons for being housebound or bedbound.	Thank you for your comment. After considering stakeholder comments this recommendation has been edited to, 'or the risk that their symptoms will worsen may prevent people from leaving their home' and hope this adds some clarity for readers.
The ME Association	Guideline	019	008 - 029	Refer to comment above about the practical aspect of implementing these measures in the NHS and whether the guideline can be used to implement such considerations in practice.	Thank you for your comment. The committee acknowledge that these aims and adaptions may not always be achievable but they should be considered and addressed where possible.

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The ME Association	Guideline	019	001 - 007	– The sections relating to hospital care should be directed at those responsible for admitting people with ME/CFS to outpatient services and inpatient appointments or for surgery etc. e.g., General Practitioners, ME/CFS specialists, paediatricians, consultants etc. – It is unclear if any of these measures – particularly those relating to inpatient care – are practically possible. – While it is appropriate to include these measures, it would help to have some idea of how likely it might be for them to occur. For example: • To what extent are ME/CFS specialist services able to adopt these measures on an individual basis? • Would admittance to hospital via ambulance likely take account of a person's needs? • Are there any hospital inpatient services who are able to cater to a person's needs? To what extent can these measures be used by a person with ME/CFS to improve the way they are treated in hospital?	Thank you for your comment. The recommendations in this section are directed at the health or social care professional discussing the person's needs with them as you note this could be one of many professionals and adding examples to the recommendations does not add any clarity for this reason your suggestion has not been added. The committee acknowledge that these aims and adaptions may not always be achievable but they should be considered and addressed where possible to improve access to care for people with ME/CFS.
The ME Association	Guideline	020	026 - 030	– What are the 'risks' associated with such advice? – It is not clear who is responsible for helping provide medical evidence to support an application or where such aids and adaptations might be obtained. Provide link to the ME/CFS severity definitions that are mentioned.	Thank you for your comment. The committee note there are risks and benefits to all strategies to support people with ME/CFS managing their symptoms and any risk, if any, will be individual to the person and should be discussed. Support for activities of daily living and increasing or maintaining independence is included in the care and support plan, access to aids and adaptions is supported through this. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.

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The ME Association	Guideline	020	019 - 022	– It is not clear who is responsible for assessing and then providing aids and adaptations. – It would be very helpful if this were the responsibility of the General Practitioner or ME/CFS specialist etc. as the present situation is far from ideal with most people having to source aids and equipment themselves. Links to funding sources and how the NHS can help, would be appreciated.	Thank you for your comment. Support for activities of daily living and increasing or maintaining independence is included in the care and support plan, access to aids and adaptions is supported through this. After considering the stakeholder comments the committee added, 'provide access to aids and adaptions' to add clarification to add that this is about signposting to support.
The ME Association	Guideline	020	001 -003	– 'Social care needs assessment' or is 'social care assessment' something different? An explanation of the terminology would be helpful. – This section should be linked with the preceding information about social care in 1.6.8. – It would help if the healthcare professional responsible/able for making an application to social care – and for completing a needs assessment if applicable – is mentioned at the start of this section e.g., General Practitioner, ME/CFS specialist, paediatrician etc. – Access to social care should be relatively straightforward and not be a barrier to care. Applications should be supported healthcare professionals. It is not clear in this section what practical measures might result from completing a social care assessment or obtaining a successful application and an explanation would help people with ME/CFS to learn the benefits and how it can help their situation.	Thank you for your comment. These recommendations now refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations. The committee note that the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan and help them access services.
The ME Association	Guideline	020	023 - 025	– Who might be responsible for the required medical or social care assessment? Links to funding sources and applicable grants e.g., the disabled facilities grant, and how the NHS can help, would be helpful here.	Thank you for your comment. These recommendations refer to the social care needs assessment and the aids and adaptions identified as part of that assessment. This has been made clearer in the recommendations.

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					The committee note that the multidisciplinary care section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan and help them access services.
The ME Association	Guideline	020	017 - 018	Who is responsible for providing this information? What are the training and resources being discussed here? Links to relevant sources would be helpful.	Thank you for your comment. The NICE guideline on supporting carers has been added and provides further information.
The ME Association	Guideline	021	003 - 010	– Who is responsible for advising people with ME/CFS about issues in relation to work, education and training? It would be helpful to know so that people are clear on who they can consult. – Include: • it may be necessary to consider early retirement on the grounds of ill-health if ME/CFS and any associated disability is unlikely to improve. • it may be necessary to reconsider any planned return to pre-illness work, education, or training, and to think about a role that is more compatible with current abilities. • where a return to work, education, or training, is being considered, it may be best to negotiate a phrased return over several months where at all possible. – Amend: • there may be long periods of absence from work, education, or training because of ME/CFS and associated disability. some people find that returning to work, education, or training too soon or without making adjustments worsens ME/CFS symptoms and can result in relapse.	Thank you for your comment. Education, training or employment support needs is included in the care and support plan. The recommendations are directed at the health or social care professional discussing the person's needs as you note this could be one of many professionals and adding examples to the recommendations does not add any clarity for this reason your suggestion has not been added. The additions you suggest are already covered within the bullet points and taking into account that any advice should be personalised no other examples have been added.
The ME Association	Guideline	021	011 - 014	– It is not clear whose responsibility it might be to offer this liaison with employers etc. and it would be helpful to know.	Thank you for your comment. Education, training or employment support needs is included in the care and support plan. The recommendations are directed at

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				– Medical evidence of sickness and disability would clearly be needed to meet statutory requirements for any absence, but it is not clear if the ongoing liaison with employers etc. is best completed by a General Practitioner or ME/CFS specialist, for example. – It would help to know the extent of the NHS's responsibility in these matters and who people with ME/CFS might turn for help. It would be useful if mention could be made of the importance of working with the person with ME/CFS and with parents where applicable or family before informing employers and education providers about their situation.	the health or social care professional discussing the person's needs as you note this could be one of many professionals and adding examples to the recommendations does not add any clarity for this reason your suggestion has not been added.
The ME Association	Guideline	021	015 - 017	– Who has responsibility for informing the education provider of a person's new diagnosis? Is this something the healthcare professional should do, or is it the parent's responsibility? It would be helpful if mention could be made of the importance of working with parents and the person with ME/CFS before informing education providers.	Thank you for your comment. Education, training or employment support needs is included in the care and support plan. The recommendations are directed at the health or social care professional discussing the person's needs as you note this could be one of many professionals and adding examples to the recommendations does not add any clarity for this reason your suggestion has not been added.
The ME Association	Guideline	022	001 - 005	It would be helpful here if mention could be made of the importance of working with parents and the person with ME/CFS before informing training and education providers.	Thank you for your comment. The committee agree that the issue of choice and consent is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan. This includes in the case of children and young people involving their parents and carers where appropriate.

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					Taking this into account no edits have been made to the recommendation.
The ME Association	Guideline	022	008 - 012	– This advice should be as applicable to adults with ME/CFS who are employed or attempting to return to work. – It should be recognised that because of financial concerns, employment is often deemed a priority and aiming for a more appropriate work/life balance may not be possible. The same can be said of education and training. – People with ME/CFS who are able to work or continue with education and training, often find their time outside of these activities is spent recuperating with minimal or no social activity. It is not a choice but a necessity. For others, a better balance is possible, but this often depends on the amount of time and effort work, education, or training might require and the impact it has on ME/CFS symptoms etc.	Thank you for the comment. The committee agree that these points could also apply to adults however they were particularly highlighted in the evidence for children and young people and the committee agreed it was important to make a recommendation highlighting this. (see evidence review A- information for people with ME/CFS)
The ME Association	Guideline	022	006 - 007	It is not clear why local authorities should possess education, health, and care plans for people with ME/CFS and not health and/or social care professionals primarily involved in the care of someone with the condition.	Thank you for your comment. An education, health and care (EHCP) plan is for children and young people aged up to 25 who need more support than is available through special educational needs support. These assessment are carried out by local authorities. https://www.gov.uk/children-with-special-educational-needs/extra-SEN-help
The ME Association	Guideline	022	018	Amend to: 'symptom management including symptom-relieving prescription medications where applicable'	Thank you for your comment. This has been edited to, 'symptom management, including prescribing and medicines management'.
The ME Association	Guideline	023	007 - 010	– This would be of significant benefit to people with ME/CFS. – This note should be made more prominent in an introduction to the guideline and elsewhere as appropriate and where we have indicated in our comments. – It attempts to deal with responsibility for ongoing care and support and people with ME/CFS need to know who to turn to when they are in need.	Thank you for your comment and information. The committee agree and the named contact is referred to in the recommendations in the flare ups and relapse and review in primary care sections of the guideline. The committee discussed whether it was appropriate to name a specific nominated professional but concluded that the most

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				– The General Practitioner should be the nominated person with overall responsibility for a person with ME/CFS's ongoing care and support and be capable of coordinating the involvement of specialists and any necessary referrals etc. – The situation with ME/CFS specialist services is often that people with the condition are referred for a set period of time and then discharged with little or no support. Ideally, continuity of care and support should be provided by these specialist services beyond discharge, but this has not been happening. It should also be noted that ME/CFS specialist services are not available to everyone with ME/CFS. Often these provisions are unavailable and Clinical Commissioning Groups (CCGs) are not providing funding either to establish a specialist service or to allow a service to provide a comprehensive provision.	appropriate professional may vary within and between across services and that this would part of local decision making. Discharge The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.
The ME Association	Guideline	023	012 - 015	– See above comments (1.10.3). – The nominated health professional in charge of continuing care and support for children and young people should be a paediatrician and/or general practitioner. Not all ME/CFS specialist services are able to provide care and support for children and young people. Most services cater only to adults.	Thank you for your comment. The committee discussed whether it was appropriate to name a specific nominated professional but concluded that the most appropriate professional may vary within and between across services and that this would part of local decision making.
The ME Association	Guideline	023	017 - 020	– It is not clear how this might apply to young people with ME/CFS. Are we talking about a transition from paediatrician care to general practitioner care? Aren't general practitioners already involved in a young person's or child's care? – It is not clear how ME/CFS specialist services differ between children, young people, and adult provision. Are these services fundamentally different? Instead of, or in addition to, providing a link to the NICE guideline on transition, it might be more helpful if the guideline on ME/CFS made it clearer what the differences are between these services	Thank you for your comment. ***Children and young people's services*** This guideline recommends that children and young people have access to the input of ME/CFS paediatric specialist services. The transition refers to adult ME/CFS services. The NICE guideline linked to on transition from children's to adults' services has more information where this is appropriate. .

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				and the extent to which children and young people's ME/CFS specialist services are available in England.	
The ME Association	Guideline	023	005 - 006	– This note should be made more prominent in an introduction to the guideline and elsewhere as appropriate and where we have indicated in our comments. – It attempts to deal with responsibility for ongoing care and support and people with ME/CFS need to know who to turn to when they are in need. – It would be helpful if the reference to 'people whose ME/CFS is managed in primary care' could be clarified. – If primary care i.e., the General Practitioner has overall responsibility for people with ME/CFS then surely everyone with the condition comes under this remit. – Reference to 'a specialist team' requires clarification. Are we talking about an ME/CFS specialist service team or something else? – It would be helpful here to have some indication as to the commitment of primary care to ongoing reviews and management of people with ME/CFS i.e., the frequency of contact that can be expected. See comments to 1.10.1 above.	Thank you for your comment. Throughout the guideline there is reference to where access to the expertise in a ME/CFS specialist team is appropriate, including confirming diagnosis, developing a care and support plan and supervision for the management of some symptoms. However the committee agreed that not everyone with ME/CFS would require or want the ongoing input from a specialist team and this is reflected in the following recommendation about the named contact being either in primary care or the ME/CFS specialist team. The named contact is the professional best placed to co-ordinate someone's care and this will be according to the person with ME/CFS circumstances. See evidence review I multidisciplinary care for the committee discussion. *Specialist team* A description of ME/CFS team has been added to the terms used in the guideline. There is information on the review of care and in the review in primary care section of the guideline.
The ME Association	Guideline	024	007 - 009	– It would help to know who should be providing this advice e.g., GPs, ME/CFS specialists etc. and any resources that professionals and people with ME/CFS might draw upon for more information. Would this be applicable to people severely and very severely affected by ME/CFS? The principles could be explained to family members or representatives when the occasion merits.	Thank you for your comment. The energy management plan is part of the care and support plan that is developed by the ME/CFS specialist team. There are additional recommendations for people with severe or very severe ME/CFS.
The ME Association	Guideline	024	002 - 003	– A link should be provided to the relevant section. We recommend that a suitable note is made in this section that warns people with ME/CFS not to assume that new symptoms or	Thank you for your comment. The recommendation on what to review includes that symptoms and any new symptoms should be discussed and after considering the stakeholder comments the committee have

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				significant setbacks in health are necessarily part of ME/CFS, but to refer to the nominated health professional for advice.	added another bullet point to ensure that any new symptoms or a change in symptoms are investigated and not assumed to be due to the person's ME/CFS. This should ensure that changing or new symptoms are not overlooked and appropriate investigations are done. This is also reinforced in the flare up and relapse section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable. As noted this point is made in different sections in the guideline.
The ME Association	Guideline	024	004 - 005	– This will be appreciated by people with ME/CFS who have faced years of inappropriate claims that, for example, if only they tried harder the treatment would work and they would be returned to health. – It will also help people with ME/CFS to realise that claims of effective treatments and of cures that are offered for sale, should be treated with caution.This note should be made more prominent in an introduction to the guideline and elsewhere as appropriate. – Include that people with ME/CFS have found pharmacological treatments helpful for symptom relief and that physicians should consider appropriate options when in consultation. – In NICE Evidence Review F Pharmacological Management, page 94, lines 30-33 it says: "The committee acknowledged that while there are not any current pharmacological treatments or cures for ME/CFS, people with ME/CFS have found some drugs when used appropriately with advice and support from health care professionals can be helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis."	Thank you for your comments. No evidence was identified for pharmacological interventions and the committee agreed they were unable to make any specific recommendations for medicines or prescribing. But as you note the committee acknowledged that while there are not any current pharmacological treatments or cures for ME/CFS, people with ME/CFS have found some drugs when used appropriately with advice and support from health care professionals can be helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis. The committee have included a section on medicines for symptom management and provided general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.

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				https://www.nice.org.uk/guidance/GID-NG10091/documents/evidence-review-6 This comment should be included in the clinical guideline because we are concerned that without it, physicians will not consider potentially very helpful pharmacological treatments for symptom relief which could lead to avoidable suffering in some cases.	
The ME Association	Guideline	025	007 - 011	– Is there an accepted pro-forma for recording these measurements that healthcare providers might use? Something that is approved for the NHS and ME/CFS management? A workbook perhaps that people with ME/CFS can then use and review with the healthcare professional.	Thank you for your comment. In the rationale section the committee recognise there was a lack of effectiveness evidence on tools to support people to self-monitor activity management. The committee decided to recommend that activity recording should be as easy as possible, and people should take advantage of tools they are already using. The committee also decided to make a recommendation for research on self-monitoring management strategies to help determine which techniques are effective.
The ME Association	Guideline	025	004 - 006	– Would like to see 'individualised' or 'personalised' energy management plan included in the above sub-heading. – It is unclear who would be charged with completing this initial – and ongoing – assessment. Would be helpful to note whose responsibility this might be e.g., GPs, paediatricians, ME/CFS specialist services. Is such an assessment suitable for people very severely affected by ME/CFS?	Thank you for your comment. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This applies to the energy management plan. The energy management plan is part of the care and support plan and is initially developed by the ME/CFS specialist team. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult and it take time to digest information. Any assessments should take into account the circumstances of the person with

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					ME/CFS and the severity of their symptoms. These issues are addressed in the Access to care section of the guideline. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation
The ME Association	Guideline	025	015 - 017	Suggest the sub-heading is re-worded to read: 'Based on the person's assessment, establish a personalised activity plan within the energy envelope that aims to maintain and/or improve quality of life.'	Thank you for your comment. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This applies to the energy management plan. The committee agreed that the aim to minimise symptoms would impact on quality of life and adding this did not add any further clarity to the recommendation.
The ME Association	Guideline	025	012	A link to suitable definitions for 'rest' and 'relaxation' would be helpful. This is the first time either term has appeared in the guideline, although both appear in subsequent sections.	Thank you for your comment. The committee agreed that rest was an important part of managing activity in people with ME/CFS. As you note the role of rest and sleep are further addressed in section 1.12. When writing guidelines there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.

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The ME Association	Guideline	025	018	Might be helpful to add a link to 'activity' and the definition that appears later in the guideline.	Thank you for your comment. This has been added in.
The ME Association	Guideline	026	001 - 007	– Remove section 1.11.8. – We do not believe this section and the bullet points are necessary. Referral to an ME/CFS specialist service is covered elsewhere and any person with ME/CFS should be able to seek further support as appropriate given the statements above and below.	Thank you for your comment. Based on the quantitative and qualitative evidence and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that

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					they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service.
The ME Association	Guideline	026	012 - 015	It would be helpful here to refer to alternative means of communication with health professionals and to acknowledge that people in this situation may not be ambulatory or able to cope with any management plan.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments and hospital stays can be difficult and in the case of people with severe or very severe symptoms who are unable to leave their homes particularly challenging. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms This is addressed in the access to care section of the guideline.
The ME Association	Guideline	026	009 -011	– Remove section 1.11.9. – We do not believe this section and the bullet points are necessary. Referral to an ME/CFS specialist service is covered elsewhere and any person with ME/CFS will be able to seek further support as appropriate given the statements above and below.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews A, F,G and H) and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are

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					supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. In line with this someone could decline a referral to a specialist ME/CFS physiotherapy or occupational therapy service.
The ME Association	Guideline	027	008 - 013	Would be helpful to include a note about being able to contact a nominated healthcare professional so that families and carers do not feel they must take on this responsibility without medical support.	Thank you for your comment. The multidisciplinary section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.

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The ME Association	Guideline	027	014 - 019	Would be helpful to include a note about being able to contact a nominated healthcare professional so that families and carers do not feel they must take on this responsibility without medical support.	Thank you for your comment. The multidisciplinary section of the guideline includes a recommendation that people with ME/CFS have a named contact to coordinate their management plan, help them access services and support them during periods of relapse. When writing recommendations there is a fine line between reinforcing information and repeating information. Too much repetition results in a guideline becoming unwieldy and unusable and for this reason your suggestion has not been added to the recommendation.
The ME Association	Guideline	027	004 - 007	It be appropriate here to include a note about assessing people in this situation at every contact for any other signs of deterioration or difficulty and seeking additional support as required.	Thank you for your comment. This section is specific to the risks of prolonged immobility and highlights the areas to address for this.
The ME Association	Guideline	027	021 - 023	Recommend the sub-heading is reworded as follows: 'Do not advise people with ME/CFS to undertake aerobic or vigorous exercise, such as telling them to go to the gym, because this is likely to worsen their symptoms.'	Thank you for your comment. After considering the stakeholder comments this has been edited to, 'do not advise people with ME/CFS to undertake exercise that is not part of a programme overseen by a ME/CFS specialist team, such as telling them to go to the gym or exercise more, because this may worsen their symptoms.'
The ME Association	Guideline	028	012 - 015	– Recommend the sub-heading is reworded as follows: 'Only consider cautiously increasing physical activity for people with ME/CFS whose symptoms have stabilised and who feel ready to incorporate physical activity into their management plan.' Include link to definition of physical activity.	Thank you for your comment. This recommendation refers to the discussion between the person with ME/CFS and the ME/CFS specialist physiotherapist or occupational therapist about considering a collaborative physical activity or exercise programme under the circumstances listed. The later recommendations in this section include further detail on how increasing physical activity should be addressed.

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The ME Association	Guideline	028	019 - 022	– Research in this area has been on graded exercise therapy, and not physical activity programmes. It would be helpful to substantiate these claims, although the cautionary statement is needed and very welcome.	Thank you for your comment. Evidence review G includes the evidence for physical activity including graded exercise therapy.
The ME Association	Guideline	028	028 - 029	This point is no clear. Suggest rewording to read: 'be easily maintained before any increase in physical activity might be considered'.	Thank you for your comment. After considering the stakeholder comments this has been edited to,' maintaining this successfully for a period of time before attempting to increase it'.
The ME Association	Guideline	029	018 - 022	– Recommend a definition of 'rest' and 'sleep' is included in the guideline and linked to this section. – A good understanding of what is meant by 'rest' and 'sleep' is vital in the management of ME/CFS. – Suitable rest and good periods of sleep should be central aims of anyone trying to manage the condition, but such aims are often unobtainable, and help will be required from specialist services. – The bullet points imply that the healthcare professional providing this advice is an expert in ME/CFS management and this may not be the case. – Medications and other treatment options for managing sleep dysfunction should be specified as approaches that nominated healthcare professional might want to consider. – The lack of specific clinical trial evidence for sleep treatment in ME/CFS should not prevent options being listed. The danger of not doing so is that physicians will not consider treatments and people with ME/CFS might continue to suffer extremes when this could be avoidable. Referral to sleep specialists should be considered when sleep or problems experienced during sleep are an issue e.g., suspected sleep apnoea, night terrors, insomnia etc.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice. This advice would be part of the care and support plan that is developed by the ME/CFS specialist team and they are knowledgeable about the role of rest and sleep in people with ME/CFS.
The ME Association	Guideline	029	014 -016	– Recommend rewording as follows: 'Advise people with ME/CFS that after a period of post-exertional malaise, a flare, or relapse in health, the time it	Thank you for your comment. The committee agreed that the recommendation reflects the points you make and have no added your suggestions. The

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				takes to return to previous levels of functional ability can vary from person to person.' Additional caution could be included advising people not to rush a return to previous levels of functional ability.	recommendation links to the definitions of flare-up which includes reference to PEM. The collaborative personalised programme includes recognising a flare-up or relapse early and outlining how to manage it, as part of this any strategies would be individual and agreed with the person with ME/CFS
The ME Association	Guideline	029	003 - 004	Include reference to post-exertional malaise i.e., 'recognise post-exertional malaise (PEM), a flare, or relapse early and outline how to manage more severe symptoms'.	Thank you for your comment. The recommendation links to the definitions of flare-up which includes reference to PEM. The recommendation links to the definitions of flare-up which includes reference to PEM.
The ME Association	Guideline	029	006 - 007	Include reference to post-exertional malaise (PEM) in the sub-title.	Thank you for your comment. The recommendation links to the definitions of flare-up which includes reference to PEM.
The ME Association	Guideline	029	008 - 009	– The reference should be to ME/CFS specialist services. Not all such services have physiotherapy involvement, but they should have the required expertise or be able to refer to physiotherapy if required. Physiotherapy should be provided when needed to help with muscle and joint problems and with issues relating to mobility, in a similar way that physiotherapists can help people with multiple sclerosis e.g., massage etc.	Thank you for your comment. The committee agreed that for people with ME/CFS it was important that the healthcare professionals with the appropriate clinical background and training supported any physical activity plans, here referral is to physiotherapist or occupational therapists and then it is the physiotherapist that oversees a physical activity programme, as such the appropriate professional to access for support if needed during a flare up or relapse.
The ME Association	Guideline	029	012 - 013	Does not make sense in terms of the opening statement. Suggest rewording to: 'establishing a new physical activity baseline, but only when symptoms have stabilised, previous function has been restored, and the person feels able to resume physical activity.'	Thank you for your comment. The committee did not agree this added further clarity to the bullet point and have not added your suggestion.

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The ME Association	Guideline	029	017	Rest and Sleep: There is no mention of sleep in the section that follows (it only discusses rest) and there should be appropriate guidance available to help with sleep problems.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice
The ME Association	Guideline	030	004 - 006	– It would be helpful here to include reference to diagnosis and use of the tilt-table-test and specific diagnostic options etc. as there is no clinical guideline on orthostatic intolerance or PoTS available. – General practitioners and paediatricians should be capable of making a diagnosis but referral to specialists could be required and these should be mentioned specifically. – Recommend an additional link is included in the definition of orthostatic intolerance on the NHS website that provides a more detailed explanation of postural-orthostatic intolerance (PoTS): https://www.nhs.uk/conditions/postural-tachycardia-syndrome/ Orthostatic intolerance and PoTS etc. are believed to be relatively common concerns, and not only for people with ME/CFS, therefore we recommend that NICE consider producing a guideline that might help with diagnosis and treatment.	Thank you for your comment and information. **In the suspecting ME/CFS section of the guideline orthostatic intolerance is identified as one of the symptoms that are commonly associated with ME/CFS. The committee made a consensus recommendation to raise awareness about this. The guideline is about the diagnosis and management of ME/CFS and for this reason the committee was unable to make more detailed recommendations on the causes or diagnosis of orthostatic intolerance.**
The ME Association	Guideline	030	007 - 009	– Amend. It is reasonable to expect that general practitioners and paediatricians are able to prescribe any necessary medications once a diagnosis has been made of orthostatic intolerance or PoTS etc.	Thank you for your comment. This recommendation does not exclude general practitioners or paediatricians from prescribing medications just that this should be as a minimum overseen by a healthcare professional with expertise in orthostatic intolerance.

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				– ME/CFS specialist services should be able to recognise and suggest a diagnosis of these issues as well as provide advice on treatment and management. – It would be beneficial if NICE could include specific treatment recommendations as no guideline exists for orthostatic intolerance or PoTS. Any contraindications for treatments that might exacerbate other symptoms of ME/CFS should be mentioned here.	The committee agree that care should be taken to ensure that the treatment for any coexisting condition does not exacerbate the symptoms of ME/CFS. The managing co-existing conditions of section of the guideline recommends that the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS.
The ME Association	Guideline	030	010 - 012	– It would be helpful if the speciality responsible for orthostatic intolerance in secondary care were included here so that people with ME/CFS know who might become involved. It is unclear the extent to which general practitioners and ME/CFS specialist services might be considered capable of helping to provide treatment and management advice in this regard – but this should be made clear above.	Thank you for your comment. When discussing this topic the committee noted that there is no defined speciality for orthostatic intolerance and that where to be referred can be down to local arrangements. For this reason the committee were unable to be specific about the speciality.
The ME Association	Guideline	030	001 - 002	Recommend a suitable definition of 'relaxation techniques' be included in the definitions section below.	Thank you for your comment. No evidence was identified to support recommending specific relaxation techniques for people with ME/CFS (Evidence reviews G,H and I) and the committee agreed they could not include any specific techniques but the committee recognised that some people find using relaxation helpful.
The ME Association	Guideline	030	015 - 016	– People with ME/CFS need to know how they can cope with pain and what options are available to them including pharmaceutical help and any alternative suggestions. – Providing two links to existing NICE guidelines on generic management of certain types of pain is not enough to justify the title: managing pain. – People with ME/CFS and healthcare professionals will expect this guideline to provide a complete review of e.g., symptom management and this should include the types of pain commonly encountered including muscular aches and pains, unusual headaches, migraines, joint pain etc. even where clinical trial evidence for use in ME/CFS is not available.	Thank you for your comment. Pain relief was included as an intervention in the protocol for pharmacological interventions. No evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee agree that people with ME/CFS report many different types of pain. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the

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				Healthcare professionals should be directed to consider all options available to manage pain and not leave people with ME/CFS to struggle through pain without help.	'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.
The ME Association	Guideline	030	014	– This section is wholly inadequate and provides little help for people with ME/CFS. The pain that occurs as a result of this condition requires acknowledging and an appreciation of the difficulties encountered when trying to live with it. Healthcare professionals should be directed to consider appropriate prescription medications and alternatives and not leave people with ME/CFS to struggle through pain without help.	Thank you for your comments. Although pain relief was included in the protocol for pharmacological interventions no evidence was identified and the committee agreed they were unable to make any recommendations for specific medications. The committee linked to NICE guidance that was relevant to people with ME/CFS, the committee acknowledged that this does not address all the type of pain that people with ME/CFS may experience. The committee agree that care for people with ME/CFS should be personalised and recommend a personalised care and support plan in the assessment and care planning section of the guideline. Management of pain should be part of the personalised plan. The committee have noted at the beginning of the managing ME/CFS section and 'managing coexisting conditions that the recommendations in the section on principles of care for people with ME/CFS and section on access to care and energy management should be taken into account when managing symptoms and coexisting conditions in people with ME/CFS. Taking into account the comments by stakeholders the committee have added a consensus recommendation in the 'managing pain' section of the guideline to raise awareness that pain is a symptom commonly associated with ME/CFS and should be investigated and managed in accordance with best practice and referred to pain services if appropriate.

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					The committee did provide general advice for health professionals on what to be aware of when prescribing medicines for people with ME/CFS.
The ME Association	Guideline	031	001 - 004	– It is not clear why nausea has been singled out from the list of symptoms necessary for a diagnosis of ME/CFS or from the list of additional symptoms. – Nausea warrants investigation if it is a new symptom or an existing symptom that persists and affects daily function to a significant degree. – It might be caused by feelings of vertigo, dizziness etc. or be part of the orthostatic intolerance discussed above, but it could also be caused by something else and should not be assumed to be a symptom of ME/CFS. – Treatments can be offered for nausea in addition to the basic advice in this section and these should be featured and discussed. An additional note should be included that relates to problems with the gut and bowel e.g., irritable bowel syndrome and other symptoms. These may include symptoms of nausea and a link should be included to the NICE guideline on irritable bowel syndrome (CG61) and to possible referral to a dietary specialist for additional help and advice.	Thank you for your comment. Nausea was identified by the committee as a symptom commonly experienced by people with ME/CFS and this can have an impact on maintaining a healthy diet. The committee agree that any symptoms should be investigated to rule out other diagnoses or coexisting conditions and if there is any uncertainty in interpreting signs or symptoms then advice should be sought from an appropriate specialist. In the absence of any evidence on dietary strategies or treatments for nausea the committee made a consensus recommendation with general advice (now in the dietary management section) and expanded on this in the committee discussion in Evidence review G- Non-pharmacological management. The NICE guideline on irritable bowel syndrome (CG61) has been added to the list of NICE guidelines for co-existing conditions. There are recommendations in the guideline clarifying when people with ME/CFS should be referred to a dietician with a special interest in ME/CFS.
The ME Association	Guideline	031	005 - 006	– Suggest: 'Do not offer any medicines or supplements to treat or cure ME/CFS or any presumed disease process.' – It is not clear who this cautionary note is directed at. It is helpful in that it might be of use when encountering practitioners/promoters who recommend such things to	Thank you for your comment. The recommendation is directed at anyone that offers medicines or supplements as a cure for ME/CFS. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.'

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				unwary and desperate people with ME/CFS, but it would be better to include an explanation. This section could be combined with a section on symptom management which may be more appropriate (see general comment above).	The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. The discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.
The ME Association	Guideline	031	008 - 009	– This appears to assume that people with ME/CFS are taking medications when many will not be aware that there are drugs that can help alleviate some symptoms. – People suspected of having the condition, the newly diagnosed, and even people who have had ME/CFS for a long time, will not necessarily be in receipt of any medication. – It would be more helpful if, as part of the care and management plan, healthcare professionals were directed to discuss symptom-relieving medications earlier in the process as part of the holistic approach. – For people who are on medications and are finding them to be an essential part of management and a vital aid to daily life with ME/CFS, medication reviews can cause alarm as they can imply a reduced prescription or change of medication. – It can often take people with ME/CFS a long time to find a drug that helps and can be tolerated. Any medicine review should take this into account and be mindful that any change can cause additional distress. This section could be combined with a section on symptom management which may be more appropriate (see general comment above).	Thank you for your comment. The recommendations on the care and support plan do link to the medicines management section in the symptom management section. A medicines review is good practice and …
The ME Association	Guideline	031	007	– This section is wholly inadequate and does nothing to suggest the kind of drugs that might help alleviate certain symptoms of ME/CFS.	Thank you for your comment. The evidence for any pharmacological interventions for ME/CFS was inconclusive with limited evidence for any one medicine and this was supported by the committee's clinical experience and

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				– It currently reads as though medications are not generally recommended at all when we know that drugs can be vital for those who are struggling with pain, sleep, or any associated anxiety or depression for example. – NICE really need to reconsider this section and how it will be interpreted by people with ME/CFS who turn to the guideline for help. – General practitioners, paediatricians, and other healthcare professionals who have the ability to prescribe medications need to be directed to the kind of drugs that might prove helpful when they are in consultation with a person with ME/CFS. – If they are not directed to drug options in this guideline, then some people with ME/CFS may not receive the help that others with ME/CFS receive – and this would be wrong. This section could be combined with a section on symptom management which may be more appropriate (see general comment above).	consensus view. As a result the committee could not confidently recommend any medicines. After considering the stakeholder comments the committee agreed the use of treatment in this context could be confusing and edited the recommendation to, 'do not offer any medicines or supplements to cure ME/CFS.' The committee note the following subsection in the guideline is 'medicines for symptom management' and provides advice for prescribers. As you note the discussion section of Evidence review F: Pharmacological management recognises some people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and this should be discussed on an individual basis.
The ME Association	Guideline	032	004 - 007	Include reference to 'appetite' and finding ways to ensure an appropriate diet and fluid intake when illness affects appetite or the ability to consume food or drink to a significant extent.	Thank you for your comment. Changes to appetite has been added to the recommendation.
The ME Association	Guideline	032	011 - 014	It would be helpful if responsibility for this consideration were included i.e., is this something a person with ME/CFS might expect their general practitioner to review regularly?	Thank you for your comment. The recommendation links to the NICE guideline on vitamin D and this provides further guidance on testing and the provision of vitamin D supplements.
The ME Association	Guideline	032	001 - 003	Dietary management and strategies should include a numbered point to cover the dietary management of gastrointestinal symptoms, bloating, pain, wind, constipation or diarrhoea and signposting to the NICE guidelines (CG 61) on Irritable Bowel Syndrome.	Thank you for your comment. The NICE guideline on Irritable bowel syndrome has been added to the guidelines listed in the coexisting conditions section of the guideline to signpost people with ME/CFS for support with these gastrointestinal symptoms.
The ME Association	Guideline	032	008 - 010	– It is not clear if such specialists with experience of ME/CFS are readily available, but this could be an opportunity to recommend they are included as a key part of an ME/CFS specialist service.	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific

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				– Include necessity of home visits by dietitian's when dealing with people severely and very severely affected who will be unable to leave their homes. – Concerns relating to malnutrition and specialist help when appetite is supressed or there is a marked inability to consume food or drink and tube-feeding etc. might be appropriate, should also form part of the expertise that may be required. It should be acknowledged that poor appetite can be linked to altered taste, smell, and texture tolerances.	dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. They are included here and in the multidisciplinary section of the guideline access to health and social care professionals with expertise in diet and nutrition is included. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
The ME Association	Guideline	032	021 - 023	– It is not clear if such specialists with experience of ME/CFS are readily available, but this could be an opportunity to recommend they are included as a key part of an ME/CFS specialist service.	Thank you for your comment. The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS.

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				– Include necessity of home visits by dietitian's when dealing with people severely and very severely affected who will be unable to leave their homes. – Concerns relating to malnutrition and specialist help when appetite is supressed or there is a marked inability to consume food or drink and tube-feeding etc. might be appropriate, should also form part of the expertise that may be required. It should be acknowledged that poor appetite can be linked to altered taste, smell, and texture tolerances.	The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. They are included here and in the multidisciplinary section of the guideline access to health and social care professionals with expertise in diet and nutrition is included. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
The ME Association	Guideline	033	006 - 014	– Include 'the severity of ME/CFS symptoms' as an option/reason for being at risk. Prolonged illness particularly of a severe or very severe nature can and does lead to problems with appetite, weight loss, and malnutrition, etc.	Thank you for your comment. The committee agree that all people with severe and very severe ME/CFS are at risk and recommend an assessment by a dietician with a special interest in ME/CFS. Other reasons for monitoring would be identified as part of this assessment.
The ME Association	Guideline	033	015 - 023	– This section and the bullet points should also recognise that for severely and especially very severely affected people with ME/CFS, it may not be possible to feed themselves and this responsibility will necessarily be delegated to a family member or support worker.	Thank you for your comment. The recommendation on the impact of symptoms that people with severe or very severe ME/CFS experience highlights that symptoms may mean they unable to eat and digest food easily and may need support with hydration and nutrition. The

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				Advice and support needs to be made available to family members and carers in this situation and experienced professionals should be on call to help from the ME/CFS specialist service for example.	discussion section in Evidence review G-non pharmacological management notes that in the committee's experience support could be provided by a family member and they require support and education.
The ME Association	Guideline	033	001 - 002	– What about food allergies and sensitivities in adults? – It is not clear if such specialists with experience of ME/CFS are readily available, but this could be an opportunity to recommend they are included as a key part of an ME/CFS specialist service. – Include necessity of home visits by dietitian's when dealing with people severely and very severely affected who will be unable to leave their homes. – Concerns relating to malnutrition and specialist help when appetite is supressed or there is a marked inability to consume food or drink and tube-feeding etc. might be appropriate, should also form part of the expertise that may be required. It should be acknowledged that poor appetite can be linked to altered taste, smell, and texture tolerances.	Thank you for your comment. *Allergies* This recommendation links to the NICE guideline on food allergies in children, there isn't a NICE guideline on food allergies in adults. This recommendation doesn't assume these do not exist in adults. *People with severe or very severe ME/CFS* *Specialists* The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as

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					online communications may be more appropriate depending on the person's symptoms. *Expertise* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *Appetite* This bullet point has been slightly reworded to include texture.
The ME Association	Guideline	033	004 - 005	– It is not clear if such specialists with experience of ME/CFS are readily available, but this could be an opportunity to recommend they are included as a key part of an ME/CFS specialist service. – Include necessity of home visits by dietitian's when dealing with people severely and very severely affected who will be unable to leave their homes. – Concerns relating to malnutrition and specialist help when appetite is supressed or there is a marked inability to consume food or drink and tube-feeding etc. might be appropriate, should also form part of the expertise that may be required. It should be acknowledged that poor appetite can be linked to altered taste, smell, and texture tolerances.	Thank you for your comment. *People with severe or very severe ME/CFS* *Specialists* The committee agree there is a lack of dieticians in the NHS that specialise in ME/CFS but consider that in their clinical experience and consensus view people with ME/CFS can have specific dietary management needs that require access to a dietician who understands the needs of people with ME/CFS. The recommendation has been reworded to describe dietician as a 'dietician who has a special interest in ME/CFS', the committee recognised that currently dieticians are not solely based in ME/CFS services (specialising in ME/CFS) but there are dieticians that provide expertise to ME/CFS services, special interest describes this group of professionals better. *Home visits* The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe

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					ME/CFS. Home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. *Expertise* The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. *Appetite* This bullet point has been slightly reworded to include texture.
The ME Association	Guideline	034	009 - 020	– Refer to general comment above and concern about over-promotion of CBT. The same considerations could equally apply to any form of psychological support and not just CBT for ME/CFS.	Thank you for your comment. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The ME Association	Guideline	034	021 - 029	– We are concerned that this section implies in part that CBT is about more than helping people cope with the effects that ME/CFS can have on a person's mental health. – It is not clear the extent to which NICE are including CBT with earlier guidance on the preparation of a management plan and with energy management strategies.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage

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				Psychological support should be aimed primarily at helping people cope, to adapt, and to accept ME/CFS and the effect it has on someone who was previously healthy.	their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After considering the range stakeholder comments about the title not being representative of this section the committee edited the title of this section to remove psychological support recognising this only referred to CBT.
The ME Association	Guideline	034	002 - 005	– Refer to general comment above and concern about over-promotion of CBT. This section could equally apply to any psychological support offered by a qualified therapist with experience of ME/CFS.	Thank you for your comment. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The ME Association	Guideline	034	006 - 008	– Refer to general comment above and concern about over-promotion of CBT. The same consideration (re: experience and supervision) is not afforded in the earlier discussions relating to management plans when perhaps it should be.	Thank you for your comment. *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence

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					reviews G and H for the evidence and the committee discussion on these recommendations). Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. The committee have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited.
The ME Association	Guideline	035	001 - 013	– We are concerned that the CBT described here seems to be aimed primarily at ME/CFS symptom management and not aimed at addressing associated mental health challenges. – People with ME/CFS will have many things preying on their minds and causing distress e.g., loss of career, income insecurity, relationship concerns, which might compound a person's overall health, but they can be treated as mental health problems. – Psychological support should enable people to offload, to receive help learning techniques that might help them deal with issues about which they might not have any control. It should be part of any holistic management approach, but not primarily aimed at ME/CFS symptom management.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness.

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The ME Association	Guideline	035	018 - 021	Refer to general comment above and concern about over-promotion of CBT.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The ME Association	Guideline	035	023 - 026	– Refer to general comment above and concern about over-promotion of CBT. Consider how mental health therapy might best be delivered to people housebound and/or bedbound and unable to leave their homes i.e., consider home visits, telephone or video consultations etc.	*Thank you for your comment.* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe

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					ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms.
The ME Association	Guideline	035	015 - 017	Refer to general comment above and concern about over-promotion of CBT.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The ME Association	Guideline	036	007 -011	– These are not the only co-morbidities that people with suspected or diagnosed ME/CFS might have and that healthcare professionals need to consider and of those mentioned several should also be considered exclusionary diagnoses. – It is important that healthcare professionals are made aware of conditions that can be diagnosed separately to ME/CFS and can exist as a co-morbidity, for which effective treatments might be afforded, at an early stage in the diagnostic process. – It should be noted that thyroid disease and coeliac disease are not common comorbidities although they might share symptoms that are similar to ME/CFS and can warrant	Thank you for your comment. Evidence review D- Diagnosis includes comprehensive lists of differential and co-existing conditions that are commonly associated with ME/CFS. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not infer any importance of the condition in reference to co-existing with ME/CFS. After considering the stakeholder comments the committee removed the reference to the NICE guideline on Coeliac disease and added the NICE guideline on irritable bowel syndrome in adults.

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				exclusions as part of the diagnostic process especially where treatment is seen to resolve symptoms. – Some people with ME/CFS self-prescribe a gluten free (GF) diet which they believe helps related gut symptoms and such symptoms could be mistaken for coeliac disease. But, in our experience, ME/CFS rarely co-exists with coeliac disease. – It should be noted that while some people with ME/CFS may have a co-existing diagnosis of Thyroid disease, this may also be an exclusionary diagnosis especially treatment is seen to resolve symptoms.. – It would be appropriate to mention co-existing IBS symptoms and signpost to NICE guidelines (CG61). – This short list fails to include e.g., Fibromyalgia (FM), irritable Bowel Syndrome (IBS), Ehlers-Danlos Syndrome, Hypermobility, Migraine, and other more commonly reported conditions and co-morbidities. If co-existing conditions are readily identified then relevant treatment and advice can be afforded that could help to relieve symptoms and improve quality of life for people with ME/CFS.	
The ME Association	Guideline	036	001 - 004	– Please refer to our general comment above in respect of section 1.2.2 and the recommendation that a section on exclusionary and comorbid conditions be included much earlier in the guideline. – This is the first time co-existing conditions (co-morbidities) have been mentioned in the guideline and healthcare professionals should be aware they must be considered at the time ME/CFS is suspected, diagnosed, as part of any ongoing medical review, or when new symptoms occur. At the very least a link earlier in the guideline should inform healthcare professionals and people with ME/CFS that this latter section is available and should be considered before a diagnosis is made etc.	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. After considering the stakeholder comments the committee have now included examples of investigations that might be carried out. In addition a recommendation on assessing new symptoms has been added to the review in primary care section of the guideline to reflect this.

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					After reviewing the structure of the guideline and taking into account the changes above the committee agreed that this section was appropriately placed.
The ME Association	Guideline	036	012 - 013	– These are not specific to ME/CFS and any mental health problems as a result of trying to cope with the condition. A link should be made with 'psychological support' in section 1.11.43 above.	Thank you for your comment. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not infer any importance of the condition in reference to co-existing with ME/CFS.
The ME Association	Guideline	037	006 - 013	– Post-exertional malaise could be a trigger for a flare in symptoms. – While people with ME/CFS should reduce activity levels – they often do not have a choice. – It would be helpful if NICE could suggest what other actions people might take in these circumstances e.g., with regard to rest and relaxation and reducing or delegating or postponing responsibilities. – The likely effect on family, work, education, training etc. should also be addressed e.g., reduced commitments and the effect of sickness absences. There is no reference here to illness severities and the possibility that a flare could result in someone with severe ME/CFS becoming very severely affected or someone becoming housebound or bedbound etc.	Thank you for your comment and information. This section is about managing a flare up* and relapse and the strategies to address this. The definition in the terms used in the guideline on flare up includes reference to PEM recognising that flare ups usually occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM. The recommendation includes general strategies for people with ME/CFS, specific strategies such as delegating responsibilities and the impact on work would be individual to the person with ME/CFS and discussed as part of their care and support plan. The risk of including examples in a recommendation is that they cannot be exhaustive and there is the risk these are taken as the only options available. *After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
The ME Association	Guideline	037	002 - 005	It would be helpful to include reference to post-exertional malaise in this context.	Thank you for your comment. The definition in the terms used in the guideline on flare up includes reference to PEM recognising that flare ups usually

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					occur as part of PEM but it is possible for other symptoms, such as pain, to flare up without PEM.
The ME Association	Guideline	037	015 - 017	– A relapse should prompt a complete medical review. There is no reference here to illness severities and the possibility that a relapse could result in someone with mild ME/CFS becoming severely affected etc. and the effect this can have on daily living, everyday responsibilities incl. employment and education, the need for increased support, greater reliance on aids and on carers, and on mental health for example.	Thank you for your comment and information. Review of the care and support plan after relapse is included in this section. This section is about managing a flare up* and relapse and the strategies to address this. * After considering the range of stakeholder comments on the terms flare and relapse the committee agreed to change flare to flare up and not to edit relapse.
The ME Association	Guideline	037	002	This section seems to be aimed primarily at people with ME/CFS and not healthcare professionals. We would recommend that healthcare professionals are just as involved in helping provide support during these periods when consultations may be especially welcome.	Thank you for your comment. The committee agree and in this section include recommendations to contact their named contact for support.
The ME Association	Guideline	039	008 -020	– This is the first-time reference to a discharge letter from ME/CFS specialist services has been mentioned. It should be included as part of the process when people make use of any service in their area and be a feature of the section on ME/CFS specialist service referrals. – Include discussion of disability and out of work benefits (Personal Independence Payment, Employment and Support Allowance, Universal Credit) as well as NHS continuing care and social care support in the review. – Healthcare professionals should be encouraged to support any proposed application and to make suggestions where appropriate given current circumstances. Include a review of medications but refer to our comments and concerns above. New prescriptions should be considered if symptoms and symptom severity warrant them.	Thank you for your comment. The committee agree that good communication is important between services and have emphasised this in the guideline. The recommendations in the review section of the guideline include the minimum areas for assessment and documentation for all people with ME/CFS. This is not intended to be an exhaustive list and should be tailored according to the individual. These areas can be used as the basis for a discussion on accessing disability support where appropriate. The committee noted in Evidence review J: Review of Care that written assessments, and reassessments, are important for accessing disability support and a scheduled review is such an opportunity.

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					The medicines section of the guideline recommends that people with ME/CFS should be offered a medication review in line with the NICE guidelines on medicines adherence and medicines optimisation.
The ME Association	Guideline	039	023 - 025	– This section should be replicated at the beginning of the guideline when ME/CFS is suspected and/or diagnosed. Referral to specialists who have expertise in conditions/areas other than ME/CFS should form part of the diagnostic process *and* any ongoing review.	Thank you for your comment. This recommendation is duplicated in the suspecting ME/CFS and the diagnosis sections of the guidelines.
The ME Association	Guideline	039	021 - 022	Amend 'specialist team' to 'ME/CFS specialist service'.	Thank you for your comment. This has been edited to ME/CFS specialist team.
The ME Association	Guideline	040	016 - 023	– Include that any training resources should reflect the new NICE clinical guideline on ME/CFS. – It would be really helpful if training could be built upon and include reference to the information and guidance already available from The ME Association that relate to symptoms, management, disability, prognosis, and benefits, for example: https://meassociation.org.uk/product-category/medical-management/ – Training need not 'reinvent the wheel' but can draw upon the training materials recently produced by e.g., the CMRC Medical Education Group and its Online CPD Training Module for Healthcare Professionals: https://www.studyprn.com/p/chronic-fatigue-syndrome – Another excellent resource that features clinical experts in ME/CFS sharing their opinions and people with the condition sharing their experiences, is a series of high-quality videos produced as a Wellcome Trust project by Natalie Boulton and Josh Biggs: Dialogues of a Neglected Illness: https://www.dialogues-mecfs.co.uk/	Thank you for your comment. This section reinforces the importance of training being up to date and that health and social care staff deliver relevant to their role so that they provide care in line with this guideline. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme.

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				– As previously mentioned, it would help if due consideration can be given to making a series of guides available that support healthcare professionals and people with ME/CFS when describing the condition and its effects and how best to manage it. The ME Association would be happy to help with any such project. Such guides would expand on the information in the NICE guideline and could become a national standard in the NHS. The described approaches would then be tailored to the individual by ME/CFS specialist services and General Practitioners or Paediatricians etc.	
The ME Association	Guideline	041	001 - 004	– Include a suggestion of the Continuing Professional Development (hours/points) on ME/CFS that is recommended for certain key roles e.g., general practitioner, paediatrician, neurologist, ME/CFS specialist etc. A link to the Study PRN Online CPD module recently released for ME/CFS would be welcome here. It provides one hour of CPD training and was created by the CMRC Medical Education Group: https://www.studyprn.com/p/chronic-fatigue-syndrome	Thank you for your comment. The first recommendation in this section has been edited to, 'health and social care providers should ensure that all staff delivering care to people with ME/CFS maintain continuous professional development in ME/CFS relevant to their role so that they provide care in line with this guideline. '. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme..
The ME Association	Guideline	042	009 - 020	Any concerns we have with the definitions have been raised earlier in the comments above.	Thank you for your comment.
The ME Association	Guideline	043	001 - 030	Any concerns we have with the definitions have been raised earlier in the comments above.	Thank you for your comment.
The ME Association	Guideline	044	001 - 029	Any concerns we have with the definitions have been raised earlier in the comments above.	Thank you for your comment.
The ME Association	Guideline	045	001 - 020	Any concerns we have with the definitions have been raised earlier in the comments above.	Thank you for your comment.
The ME Association	Guideline	022 023	013 - 022 001 - 004	– It would be helpful to have an idea of the kind of professionals ideally involved in delivering such ongoing	The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the

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				care and support e.g., consultant specialists, GPs with a special interest, GPs, occupational therapists, psychologists, dietitians, social care professionals etc. – It is presumed that this section is concerned with ME/CFS specialist services although no mention is actually made of them or their role. It would be helpful if this were clarified. A note should also be included that in the absence of appropriate ME/CFS specialist service provision, a GP and/or paediatrician should be capable of providing and coordinating appropriate multidisciplinary care.	evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised certain parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering stakeholder comments about the requirement for medical expertise input into the care of people with ME/CFS the committee agreed to replace the term 'a comprehensive clinical history' in 1.2.2 with 'a medical assessment in the recommendations on suspecting ME/CFS, assessment and care and support planning and multidisciplinary care. This would typically require access to a ME/CFS specialist physician or a GP with a special interest in ME whilst not excluding a role for the highly trained ME/CFS advanced practitioner.
The ME Association	Guideline	046	004	We would welcome the addition of research recommendations that determined the underlying disease process(es), a better understanding of symptoms, and the development or repurposing of pharmacological treatments that better aid symptom relief and improve functionality.	Thank you for your comment. The research recommendations are developed from the evidence reviews and as evidence looking for causes and mechanisms of ME/CFS was not reviewed the committee were unable to make a research recommendation on this topic.
The ME Association	Guideline	047	007 - 015	We have no comments to make about the rationale and presumed impact other than the comments above.	Thank you for your comment.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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The ME Association	Guideline	024 025	010 - 024 001 - 003	– Would like to see reference to 'Pacing' which is the commonly used term best describing energy management. – Would like to see reference to effective use of rest, relaxation, distraction, sleep etc. as part of an 'energy management plan'. – Is it possible to include a link to a recommended written explanation of Pacing/Energy Management that includes some examples? A resource that the committee might endorse. It would help both general practitioners and people with ME/CFS if a suitable resource could be accessed providing more information as the overview provided in the guideline for what amounts to the main form of management is not sufficient.	Thank you for your comment. The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.
The Pituitary Foundation	Guideline	004	010 - 011	This is equally true of pituitary disease which should be ruled out.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
The Pituitary Foundation	Guideline	004	013 - 014	Awareness that pituitary conditions can have similar symptoms, so need to be ruled out	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
The Pituitary Foundation	Guideline	005	009 - 011	Testing of pituitary hormones to rule out pituitary disease. When GP's trying to diagnose, thyroid testing is carried out, but no	Thank you for your comment.

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				mention of other hormones. Suggest cortisol, prolactin, growth hormone, oestrogen & testosterone also tested.	Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
The Pituitary Foundation	Guideline	006	014 - 016 018 - 021 024 - 025	People with pituitary disease may experience these symptoms, therefore specific testing of pituitary hormones is important to rule this out.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The importance of using clinical judgment when deciding on additional investigations is emphasised. The examples are not intended to be an exhaustive list.
The Pituitary Foundation	Guideline	032	021 - 023	Testing of pituitary hormones to rule out hormone deficiencies which may cause growth problems in children should be considered at diagnostic stage.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
The Pituitary Foundation	Guideline	050	009 - 012	Pituitary disease should also be considered if ME/CFS is suspected and referral made to an Endocrinologist if necessary.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The importance of using clinical judgment when deciding on additional investigations is emphasised. The examples given are not intended to be an exhaustive list. In addition the committee are clear that primary healthcare professionals should consider seeking advice from an

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					appropriate specialist if there is uncertainty about interpreting signs and symptoms and whether an early referral is needed.
The Royal College of Nursing	General	General	General	The Royal College of Nursing (RCN) welcomes the opportunity to review and comment on the NICE Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management guidelines. The RCN invited comments from members who care for people with this condition and / or have knowledge of this condition.	Thank you for your comment.
The Royal College of Nursing	Guideline	016	005 - 015	"1.7 *Safeguarding* *1.7.1 Safeguarding assessments in people with confirmed or suspected ME/CFS should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS.* *1.7.2 Recognise that people with ME/CFS, particularly those with severe or very severe ME/CFS, are at risk of their symptoms being confused with signs of abuse or neglect.* *1.7.3 If an assessment under the Mental Health Act 1983 or the Mental 13 Capacity Act 2005 is needed, involve health and social care professionals who have training and experience in ME/CFS. This should be done within 24 hours in an emergency"* We would suggest that the assessment should be undertaken jointly between a health expert in safeguarding children and young people and a member of the specialist ME/CFS team as there could well be issues related to abuse or neglect. We would strongly suggest that NICE amend the NICE guidelines and recommendations accordingly.	Thank you for your comment. After considering the stakeholder comments the committee agreed to edit this recommendation to, 'directly involve health and social care professionals who have training and experience in ME/CFS'. We hope this adds clarity that this not carried out by one professional.
The Royal College of Psychiatrists	Appendix 3 – Expert testimonies	006 - 014		Professor Jonathan Edwards was asked to give evidence on the methodological issues around non pharmacological trials and outcomes. His main contribution concerned non- blinded interventions and what he called "subjective" outcomes (which we prefer to call "patient reported"), contrasting them unfavourably with those that he considered to be "objective".	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion.

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				His argument is that trials that are unblinded and have self-reported outcomes cannot be trusted or used. Because some unblinded trials are not replicated by subsequent blinded ones, which is true, then all unblinded trials are not replicated, which is not true. His point is that patients who main symptoms are self-reported do not give an accurate account of those symptoms after any intervention which is non-blinded. For that reason objective measures, such as biomarkers, exercise testing and so on, which are superior to self-report measures, could be used. We do not accept this. Indeed, the general direction of travel is more in the opposite direction – for example in responding to the views of patients about what matters to them, NICE and others have steadily increased, not decreased, the importance of self-reported outcomes, also known as Patient Reported Outcome Measures (PROMS). The issues around complex interventions that cannot be blinded has been addressed in the MRC Guide to Assessing Complex Interventions, used by most triallists in this field. He also did not mention that these issues are already included in the Grade System as outlined in the Methods Section of this review, including both unblinding and performance bias. Instead he implied that his views represented something new and additional for the committee to take into account. Do NICE agree?	The committee acknowledged in his testimony the lack of existing objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations. The committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations.
The Royal College of Psychiatrists	Appendix 3 – Expert testimonies	006 - 014		Professor Edwards considers that sufferers from ME/CFS are particularly likely to be influenced by subjective bias: "*In addition, despite some claims to the contrary from authors of ME/CFS trials, ME/CFS is usually considered a high-risk condition in terms of subjective bias. That has to be the case if psychological factors are thought to be important in symptomatology; when I mentioned facilitating a drug trial for*	Thank you for your comment. Professor Edwards was invited to provide to the committee his expertise on some of the methodological controversies in undertaking research in his area. His testimony describes and reflects his opinion.

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				ME/CFS to the head of medicine at UCH his only comment was that for ME/CFS we would need to be 100% sure of blinding." His "claims to the contrary" is a systematic review of the placebo effect in ME/CFS https://pubmed.ncbi.nlm.nih.gov/15784798/. "In contrast with the conventional wisdom, the placebo response in CFS is low. Psychological-psychiatric interventions were shown to have a lower placebo response, perhaps linked to patient expectations". This finding casts doubt on his main thesis, which is that "subjective outcomes are to be particularly distrusted in trials of CBT and GET in ME/CFS" - the evidence points the other way. Could NICE please comment?	The committee acknowledged in his testimony the lack of existing objective outcome measures of effectiveness for interventions for ME/CFS and the limitations of subjective measures. The committee discussed these methodological issues and recognised they are challenging in conducting complex interventions and are not just related to ME/CFS. All of the additional evidence enabled the committee to consider and discuss a wider range of evidence, including that from, published peer review quantitative and qualitative evidence. To note that expert witnesses are not members of the committee and are not involved in the final decisions or influence the wording of recommendations. The committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations.
The Royal College of Psychiatrists	Appendix 3 – Expert testimonies	2.3		Second Dr Husain spoke about co-morbid depression and increased risk of suicide. He said that co-morbid depression is common and can make it harder for people to improve hence needs to be treated as well. Dr Husain confirms that this was in his slides and his verbal evidence. But it seems that any mention of depression has been removed from the summary of his evidence, with only emotional wellbeing included. Emotional wellbeing is not the same as depression The College notes that the omission of depression from the guidelines is a repeated issue through the Review.	Thank you for your comment. Dr Husain's written statement is in Appendix 3 _Expert testimonies and Dr Husain's observations on mood disorders are included. There is no reference to emotional well-being in Dr Husain's written summary or in the summary of his testimony in Evidence review I_ Multidisciplinary Care. After further contact with Dr Husain the summary of his presentation to the committee in Evidence review I has been edited to include, 'Dr Husain commented that it is important to ensure other causes of fatigue are considered and to assess for

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				This is a major failing, not in the interest of patients, nor in the interest of health professionals, Depression is part of the differential diagnosis, a major comorbidity, is associated with poor outcome and poor quality of life, and is also a known risk factor for suicide, the risk of which is higher in those with ME/CFS seen in secondary care Why was it decided not to include Dr Husain's observations on suicide and depression?	mood disorders, such as depression which are common in long term conditions'. The committee discussion section in Evidence review C_ Access to care includes the following text,' "The committee noted that the experience of living with severe symptoms can significantly affect a person's emotional wellbeing and the committee commented that people with ME/CFS, particularly those with severe or very severe may be at higher risk of depression and suicide and healthcare professionals people caring for this population need to be aware of this." Also to note that after taking into consideration the stakeholder comments the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
The Royal College of Psychiatrists	Appendix 3 – Expert testimonies Evidence Review	2.3 I	2.3 22	Dr Husain, a member of this College, also gave evidence. His evidence is not in the Expert Witness section, for an unknown reason, but instead is summarised within the report on MDTs. (Page 22 ; Evidence Review 1.) This reflects what he said, but with two exceptions. Dr Husain did not say that there was a "mismatch" between patients and service providers, which clearly meant that patients did not wish to see psychologists/psychiatrists. He said the opposite – namely that most patients attending the MDT service he described did not have such problems and were happy to accept an offer of help. The committee have added their own view, not Dr Husain's, which was based on his own experience of just such a service. Could NICE explain why it was decided not to include Dr Husain's observations in full as with the other experts, and	Thank you for your comment. Dr Husain's written statement is in Appendix 3 _Expert testimonies. The comment on mismatch was part of the committee discussion that was prompted by Dr Husain's presentation and it is not attributed to him. To clarify, 'The committee noted this was not a specific comment about SLAM.' has been added to this paragraph.

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				second how what he said was turned around, so that what he actually said, namely that in this large service patients did not show evidence of "mismatch" and were pleased to receive offers of help, was lost and replaced with the opposite	
The Royal College of Psychiatrists	Evidence Review D Diagnostic Criteria Evidence Review C	3.1	029	There is also inconsistency between the decision of this committee and the decisions of the Chronic Pain draft review on the topic of indirectness. There is considerable overlap between Chronic Pain and ME/CFS and similar treatment options exist for both – exercise, activity management and CBT. CBT protocols for ME/CFS were influenced by the chronic pain literature. Chronic Pain is a much more heterogeneous condition, as the Chronic Pain review make clears, compromising a much wide range of diagnostic labels than ME/CFS. So one would might expect that there would be more, not less, evidence of indirectness in Chronic Pain, if both committees interpreted indirectness in a similar way. Yet looking at the exercise therapy sections there is a divergence but in the other direction. The exercise trials in the Chronic Pain report generated 311 separate ratings on the question of indirectness but no evidence of indirectness was noted in any of the 311 ratings. By comparison the exercise therapy trials in the ME/CFS review, generated 112 ratings on the question of indirectness of which 105 were listed as "serious" or "very serious" evidence of indirectness and only 5 had no evidence of indirectness. Such a strong divergence suggests that there is evidence of inconsistency between the reviews. Can NICE explain this difference?	Thank you for your comment. *ME/CFS population* All NICE guidelines follow the process for quality assessment of the evidence as set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews for guidelines are underpinned by protocols, these are developed and agreed by the individual guideline committees using their expertise in the topic. They set out the approach for the quality assessment before the data is collected. Reasons for indirectness or what is considered direct and indirect evidence can differ between different reviews and different topics, and the possible effects on the applicability of the evidence are considered individually. The ME/CFS guideline committee agreed that PEM is central to the diagnosis of ME/CFS and as such any evidence without a PEM population $\geq$95% may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. As such the committee agreed to downgrade for indirectness. The ME/CFS population in the guideline is very specific and the committee agree that the chronic pain population is much more heterogenous and there is a wide range of diagnostic labels compared to ME/CFS. To note the Chronic pain guideline is about Primary chronic pain (not secondary chronic pain) and it include more than 10 different conditions, hence the heterogenous nature, as such you would expect to see less indirectness in the chronic pain guideline (as is the case). The committee disagree there is inconsistency in the way

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					indirectness has been applied in the guidelines. (See the methods chapter for further information on indirectness).
The Royal College of Psychiatrists	Evidence Review D	044	Table 4	Presence of post exertional malaise - the reviewers state that the Oxford criteria do not cover post exertional malaise. This is not accurate and within the glossary both post exertional exacerbations of fatigue and myalgia are described and the framework for recording is provided. ."(c) relation to exertion: if after exertion the time of onset relative to the exertion, and duration should be described." It is worth noting that the logic behind this approach was scientific rigour and that to this day post-exertional symptom exacerbation remains undefined and without any consensus criteria as to what it actually means or how it can be measured. We suggest that the emphasis on this single symptom needs to be reviewed,	Thank you for your comment. The Oxford criteria glossary instructs clinicians to record various aspects of the fatigue, including the severity, frequency, and it's relation to activity. The committee note this is specific to fatigue and PEM is not only about fatigue but all symptoms. The Oxford criteria does not specify that PEM must be present in order to make a diagnosis, it is not a compulsory feature. The committee note that it is the combination and the interaction of the symptoms in the criteria, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS.
The Royal College of Psychiatrists	Evidence review D	048	011	We are concerned that this section makes little sense- *"The diagnostic criteria have not been evaluated in terms of their measurement validity and accuracy in diagnosing ME/CFS. Without a biomarker it is not possible to definitively know if a person has or does not have ME/CFS. Without such a reference standard it is not possible to assess the measurement validity of the different criteria".* The accuracy of a diagnosis can be tested against many standards- most commonly does the patient end up with another disease explanation during follow up? The presence of biomarker is not the gold standard as, with the exception of single gene disorders, there are virtually no biomarkers that have 100% sensitivity and specificity, and therefore biomarker led diagnoses also need to be subject to follow up for outcome validity. On the contrary, there is good evidence that the overwhelming majority of patients diagnoses with ME/CFS, by any criteria, do not end up having diagnostic revision over prolonged follow up	Thank you for your comment. The committee disagree ,a diagnostic test does not exist for ME/CFS and the rest of the section on the outcomes that matter the most and the following section on the quality of the evidence add detail and explanation to the approach used. To summarise the committee choose a pragmatic approach to bypass the difficulties concerning measurement validity. If the criteria cannot, due to the lack of a reference standard, be shown to be 'correct' or 'not correct', then a reasonable option is to show that the criteria have been developed using optimal methods. This is because an unbiased, clearly reported, evidence-based and consensus-driven process utilising the expertise of patients, clinicians and researchers is most likely to lead to more clinically useful criteria. We note the Cairns and Hotopf review included studies that used various different criteria for a diagnosis of ME/CFS. The report that patients diagnosed using these criteria do not end up with a diagnostic revision does not indicate that all the criteria

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				(e.g., Cairns and Hotopf 2005 doi:10.1093/occmed/kqi013). This is the question of interest to most clinicians and patients. We suggest an approach to a case definition that is of necessity based on symptoms.	accurately diagnose ME/CFS, but only that the people studied continue to have the same symptoms included in the criteria at follow up.
The Royal College of Psychiatrists	Evidence Review D	048	031	"*This is because an unbiased, clearly reported, evidence-based and consensus-driven process utilising the expertise of patients, clinicians and researchers is most likely to lead to more clinically useful criteria*". We are concerned that the committee did not do that, but rather decided for themselves, without underpinning evidence, any methodological process or a transparent consensus process. Furthermore, whilst patient experience is of interest, it should not be the principal basis for diagnostic criteria, as they can only be expert in their own experience not that of others; and they would not necessarily be aware of the medical conditions that form a differential diagnosis.	Thank you for the comment. See evidence review D. Appendices D and E for how quality was assessed and an explanation of the method used. In summary the AGREE II tool was used and we acknowledge that although this review does not include guidelines the principles of the decision making are similar in developing consensus based diagnostic criteria and it has been used the evaluation of consensus statements. While applying the AGREE II tool and assigning a score is less useful in this context the relevant items in the domains provide a robust set of principles to measure in the consensus criteria development. Table 11 in appendix D sets out the AGREE II domains and the relevant items evaluated in this review, this includes how stakeholder involvement is evaluated.
The Royal College of Psychiatrists	Evidence Review D	049	001	*"ongoing discussion in the ME/CFS community…..usability of the criteria as a clinical tool."* Please could NICE specify what they mean by usability? For example is it speed, accuracy, predictive validity or other factors that determine 'usability'?	Thank you for your comment. Usability refers to the ease of use in practice. Section 1.2.5 in 'the other factors the committee took into account' describes this further.
The Royal College of Psychiatrists	Evidence Review D	049	014	The College would like to highlight that memory problems in ME/CFS are not specific – indeed there is a very large neuropsychological literature on this, which appears to be have been excluded in its entirety. If the committee are going to make statements on cognitive function, they needed evidence from a neuropsychologist. The key feature of many of the cognitive problems reported by patients are that they are subjective, and not found on standard bedside or clinical neuropsychological assessments. This has	Thank you for your comment. The committee agree that this should have been an example, and this has been edited to 'for example, memory problems'.

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				been known for over 25 years – see Rasouli et al, 2019 already cited for a recent view. "Brain fog" is a useful vernacular term that many patients do use to try and describe a general experience, but it is, as the Committee admit (Recommendations, page 50, line 5) non-specific, and found in many conditions, including depression. Could NICE please comment?	
The Royal College of Psychiatrists	Evidence Review D	049	026	The college were greatly concerned by the following sentence and the serious consequences that flowed from it: *"The IOM, 2015 criteria were judged by the committee as allowing a reasonable compromise between over and under inclusion of people within the diagnostic criteria. The committee acknowledged that this judgement was made in the absence of formal measures of accuracy".* We think that this decision might be unique in guideline development. Having found no evidenceto underpin a decision, nor to have even looked at predictive validity, a committee makes a strong recommendation. And then use that recommendation to underpin the exclusion of the majority of the scientific literature from their review because they 'liked the look of something'. Whilst it may be acceptable to express a preference based on face validity, when this is used to exclude over 90% of the clinical trials conducted on the topic, it is no longer possible to justify.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. All studies that met the inclusion criteria in the protocols were included in the evidence reviews. *Excluded data* No data has been excluded that has met the review protocols. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). This point we think you refer to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that includes PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported.. The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported.

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					Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Evidence Review D	049	030	Criteria agreed by the committee: *On this basis the committee agreed the criteria and recommended that ME/CFS should be suspected in people with all of these 4 key features:* *1. Debilitating fatiguability that is not the result of ongoing excessive physical, emotional or mental exertion, and is not substantially alleviated by rest.* *2. Post-exertional symptom exacerbation, which is disproportionate to the amount of exertion (cognitive, physical, emotional and, social), and can be delayed*	Thank you for your comment. *Suspecting and diagnosing ME/CFS* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. For more detail on the committee discussion about the IOM criteria and their decision to include pain as one of the commonly associated symptoms and not a key criteria see Evidence review D-Diagnosis. The committee

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				3. Unrefreshing sleep *4. Cognitive difficulties* It is unusual to conclude by defining the most restrictive definition in the literature, solely on the basis of committee opinion, and without reference to the rate of occurrence of the individual symptom, the sensitivity or specificity of the individual symptoms, the rate of co-occurrence of all four symptoms in patients and the sensitivity and specificity of all four symptoms when they co-occur. How can this be justified? There is a large literature that at least offers some guidance on this, not least in the IOM 2015 (doi.org/10.17226/19012) criteria they cite, which reported varying rates of PESE in patients with ME/CFS from 86% to 69% depending on how PESE was defined. The IOM 2015 noted unrefreshing sleep to be present in 92% of cases, and cognitive difficulties 80% to 55% depending on definition used. They do not offer data on how often an individual patient has all four symptoms. This definition is based on opinion rather than fact Can NICE please justify this decision and its implications?	agreed it is the combination and the interaction of the symptoms, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. We note that the study referenced is the study included for the IOM criteria in the diagnostic criteria review.
The Royal College of Psychiatrists	Evidence review D	050	017	The problem of defining and measuring fatigue has been studied and discussed for over 100 years – and involves disciplines as diverse as medicine, physiology, philosophy, ergonomics, industrial psychology and more. Whole laboratories have been commissioned to try and resolve this, only to close when unsuccessful. It is indeed complex, but certain things are clear. First, people use the same words in very different ways. Doctors use fatigue very differently to patients and it lacks any diagnostic specificity, being found in hundreds and hundreds of different conditions across general medicine and psychiatry,	Thank you for your comment. The committee agree that defining and measuring fatigue is complex. The committee discussed the different types of fatigue identified in the ME/CFS literature and their own experiences. There was agreement that there is a marked difference between 'normal tiredness' and the profound fatigue caused by ME/CFS and that the term fatigue does not reflect the actual symptoms that people with ME/CFS experience. The committee had hoped to add clarity to support non-specialists in ME/CFS in understanding the fatigue people with ME/CFS experience.

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				Second, but even if there are there are very few illnesses or diseases in which fatigue is not a symptom, only rarely can it be measured objectively – as in myasthenia gravis. Neurophysiologically measured fatigue has virtually no relationship to patient reported fatigue. Third, fatigue, mood and energy are closely intertwined. The literature on the phenomenon of fatigue probably runs into thousands. Self-reported fatigue correlates very closely indeed with self-reported mood, with coefficients ranging for 0.6 to 0.8. The committee decided on "debilitating fatigability" which is perfectly reasonable, but no better than any many other descriptors, and again lacking any objective criterion by which to measure it. Can NICE please justify this decision and its implications?	After considering the range of stakeholder comments on this topic the committee agreed to edit debilitating fatiguability to debilitating fatigue recognising that fatiguability did not add clarity.
The Royal College of Psychiatrists	Evidence review D	050	042	*The committee considered PESE was a term not often understood by people outside of the ME/CFS community and wanted to clarify how it should be interpreted in a recommendation."* The committee seem under the impression that post exertional malaise/ symptom exacerbation is a unique symptom of ME/CFS but in reality, it is commonly reportedin the context of fatigue associated with:- - major depressive disorder (http://europepmc.org/article/med/20035251) - multiple sclerosis (doi: 10.1097/PSY.0b013e31824152ed) - stroke (Staub et al 2000. Fatigue after stroke: a pilot study. *Cerebrovasc Dis*, *10*(suppl 2), p.62) - traumatic brain injury (doi: 10.4085/1062-6050-48.5.02) - fibromyalgia (https://pubmed.ncbi.nlm.nih.gov/8092909/) - cancer (doi.org/10.1016/j.jpainsymman.2020.02.012)	Thank you for your comment. The committee agree that PEM is recorded to be present in other conditions but note it is the combination and the interaction of the symptoms in the criteria, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. As such PEM is essential in the diagnosis of ME/CFS, although it is reported in the context of fatigue in other conditions it is not part of the criteria for diagnosis. To note, after considering the comments made by stakeholders about the potential for misunderstanding the committee agreed to change *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE.

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				- gulf war syndrome (doi.org/10.1016/j.ijpsycho.2019.11.008) - ruptured silicone implants (J Rheumatol 2003;30:2263–7). It occurs with a rate of up to 8% in healthy sedentary adults (IOM 2015 full report DOI 10.17226/19012) Given its lack of specificity can NICE now review the emphasis give to this symptom?	
The Royal College of Psychiatrists	Evidence review D	051	004	"*The committee thought it was important to provide clarity about what is meant by activity in this context. Activity refers to any effort that requires energy expenditure and includes cognitive, physical, emotional and social activity, it is not limited to physical activity.*" We agree. Mental activity can trigger the symptoms of ME/CFS in the same way that physical activity can. Indeed this observation is part of the reasoning against ME/CFS being a primary disorder of muscle, since this is not a core feature of neuromuscular conditions unless there is comorbid depression. We also agree that emotional trauma can precipitate ME/CFS, as has been shown in case control studies. But if indeed mental fatigue and fatigability after mental activity/exertion is placed on the same footing as symptoms that occur after physical activity/exertion, this does call into question some of the committee's more speculative theories on topics like 'energy envelopes', not least because the sciences of neuropsychology and exercise physiology really are rather different. We suggest that "energy envelopes" are more of a metaphor for the underlying disturbance in the perception of exertion, supported by a wide literature.	Thank you for your comment. The concept of energy limits* and accordingly the management of energy limits to avoid the boom and bust cycle that can result in worsening of symptoms is not speculative and are well established in the care of people with ME/CFS. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit *Energy envelope to use energy limits.* The committee have added that the energy limit is the amount of energy a person has to do all activities without triggering an increase *or worsening* of their symptoms. This is linked to terms used in the guideline with further explanation of the meaning.
The Royal College of Psychiatrists	Evidence review D	053	009	"*Based on their experience the committee decided that ME/CFS should be initially suspected in people who have the four key features (debilitating fatiguability, post-exertional symptom exacerbation, unrefreshing sleep and cognitive difficulties) for a*	Thank you for your comment. As you note the committee decided that it would be unusual for all the symptoms in the criteria to be present and the following

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				minimum of 6 weeks in adults and 4 weeks in children and young people. The rationale behind this was that it would be unusual for an acute illness, including a viral illness to persist longer than this with all the symptoms" There is an extensive literature on this and they would have found that approximately 27% of patients post EBV are still symptomatic after 3 months (doi:10.1136/bmj.38933.585764.AE, https://doi.org/10.1080/21641846.2018.1426086). There are plenty of other studies of post infectious fatigue syndromes that the committee might have consulted, including those that look at predictors of chronic fatigue and CFS after infection, rather than again rely on their experience. No doubt the rapidly growing post Covid literature will soon give more examples.	sentence in the discussion text is ,'The committee emphasised it is the combination and interaction of the symptoms that is critical in distinguishing ME/CFS from other conditions and illness'. The committee agree that post viral fatigue may last longer but this is not what is being described in this guideline.
The Royal College of Psychiatrists	Evidence review D	056	020	"*The committee have recommended that diagnosis is confirmed by a specialist team."* What is a specialist team and who needs to be in it? The draft NICE guideline on the management of post-covid syndromes for a good description of such a team, based on specialists to ensure accurate diagnosis working with specialist therapists to provide evidence-based rehabilitation interventions. The college are also concerned as to whether the committee have considered the impact of their review on the commissioning of specialist teams for ME/CFS. Most specialist teams in the UK are commissioned to provide rehabilitative treatment. If commissioning follows NICE advice, these services will cease to have a purpose. Furthermore, it is far from clear whether staff trained in rehabilitation would wish to work in a service where their core	Thank you for your comment. Evidence review I _Multidisciplinary care describes the evidence and the committee discussion on the composition of an MDT and the expertise needed for the effective care of people with ME/CFS. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS. The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F

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				skills were not allowed to be utilised. Is the commissioning of specialist teams that are unable to offer treatment, based on best evidence, either practical or realistic? Why would anyone want to work in a service that, after making a diagnosis, was prevented from giving treatments they know could help? So the end result might be the unintended consequence of being even more off-putting to the majority of clinicians in UK (anecdotally the commonest response when ME comes up as a topic in medical circles is 'best just to not get involved'). Those psychiatrists who replied to our call for evidence for this consultation actually expressed the opposite view – that this was an area that it was good to be involved in, that the clinical work was very satisfying and the feedback from patients very good, as Dr Husain told the committee when he gave evidence, even if that portion of his testimony was misrepresented in the report. (Evidence Review I page 22, line 33). But nevertheless, there is no getting away from the uncomfortable and sad reality that few health care professionals seem keen to get involved in ME/CFS work, and it is hard to see how the current guidelines will improve this, and more likely the reverse	and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. The management section of the guideline sets out the interventions for supporting people with ME/CFS to manage their symptoms, including if appropriate programmes for physical activity and exercise. See the Evidence reviews Fand G for the committee discussions of the evidence. *Misrepresentation of Dr Husain's testimony* Please see comments 24 and 25.
The Royal College of Psychiatrists	Evidence review D	057	019	*"This has led to misdiagnosis, missed diagnosis, delays in the diagnosis of ME/CFS and of other conditions"* There is good evidence that diagnoses of ME/CFS are rarely revised owing to emergent pathophysiological conditions. It is disappointing that NICE did not review this literature when considering diagnostic criteria. Could NICE please review this literature ?	Thank you for your comment. We think the good evidence you are referring is the review by Cairns and Hotopf in comment 53. As in our response to comment 53 we note that the Cairns and Hotopf review included studies that used criteria that do not include PEM as essential for a diagnosis of ME/CFS and in line with this guideline could include people that would not be diagnosed with ME/CFS. We note the Cairns and Hotopf review included studies that used various different criteria for a diagnosis of ME/CFS. The report

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					that patients diagnosed using these criteria do not end up with a diagnostic revision does not indicate that all the criteria accurately diagnose ME/CFS, but only that the people studied continue to have the same symptoms included in the criteria at follow up. In the committee's clinical experience (and as suggested in stakeholder comments)- many referrals to a ME/CFS specialist team for suspected ME/CFS result in a different diagnosis. As such it is important that non-specialists in ME/CS are given clear criteria to suspect ME/CFS and the committee hope the advice on how to suspect ME/CFS and the referral for the confirmation of diagnosis by a ME/CFS specialist team will reduce the rates of misdiagnosis and missed diagnosis.
The Royal College of Psychiatrists	Evidence review D	058	001	This is the committee's proposed differential diagnosis, presumably included to guide the clinician who is seeing a patient with symptoms such as chronic fatigue not relieved by rest but made worse by exercise, physical and mental, concentration difficulties, other somatic symptoms such as pain, poor unrefreshing sleep and so on. *Endocrine, nutritional and metabolic disorders: including thyroid disorders, primary and secondary adrenocortical insufficiency, Haemochromatosis, chronic kidney disease, vitamin deficiencies* • *Genitourinary system disorders: chronic bladder infection, chronic vulvar pain* • *Auto-immune and inflammatory disorders: including primary Raynaud's, systemic 6 lupus erythematosus, Sjogren's syndrome, vasculitis, inflammatory bowel disease, 7 coeliac disease, primary biliary cirrhosis, sarcoidosis, kidney disease; endometriosis* • *Infections and infection- related disorders: including HIV, chronic viral hepatitis, tuberculosis, Lyme disease and post-Lyme*	Thank you for your comment. The committee have revised the list of differential diagnosis in evidence review D and added, mental health conditions: anxiety, depression or mood disorders.

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				syndrome, other chronic infections 10 including those rare in the UK. Also, recurrent infection associated with immune deficiency disorders • *Neurological disorders: including multiple sclerosis and myasthenia gravis* • *Cardiorespiratory disorders: including cardiac failure, chronic obstructive pulmonary disease, respiratory failure, chronic endocarditis* • *Haematological disorders: anaemias, lymphoma, chronic leukaemia, myeloma* • *Malignant disease: particularly those cancers which are often not easy to detect such as ovarian carcinoma* • *Sleep-wake disorders: including obstructive sleep apnoea and narcolepsy* • *Other chronic pain and multisystem disorders: including fibromyalgia and hypermobility spectrum disorder.* • *Iatrogenic conditions: particularly side effects of medications used for chronic pain.* It's a comprehensive list. Except for one thing. There is no mention of psychiatric conditions, for which a large literature exists to confirm that these are most commonly encountered conditions that are part of the differential diagnosis of ME/CFS in the primary or secondary care situation. Not to mention this renders any guidance or advice on diagnosis completely unfit for purpose and seriously misleading The College regards this as an extraordinary oversight. This Guideline is not fit for purpose and is it is genuinely risky.	
The Royal College of Psychiatrists	Evidence review D	058	033	"*When broader criteria are applied more people are diagnosed with ME/CFS, reducing the chances of a missed diagnosis of ME/CFS but increasing the number of false diagnoses.*"	Thank you for your comment. In the committee's clinical experience (and as suggested in other comments (see Newcastle-upon-Tyne Hospitals NHS Foundation Trust (comment 44) BACME(comment 772)) up to

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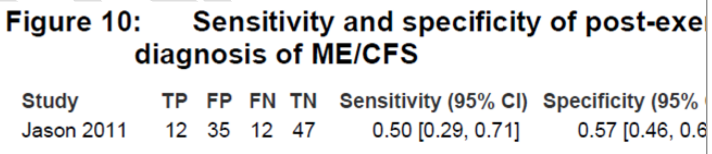
				The college is concerned that no evidence is produced to support this claim. The only data we are aware of is over-diagnosis when diagnosis is self-determined; approximately half of patients self-diagnosing ME/CFS recruited from support groups were found not have the condition on medical assessment). We are unaware of any evidence to support the statement that one set of diagnostic criteria lead to higher rates of over-diagnosis. More restrictive criteria will automatically lead to fewer patients fitting the criteria but that is not the same as over-diagnosis. Indeed, what evidence we are aware of suggests the opposite may be the case (doi:10.1017/S0033291705005210). Elsewhere in the guidance the committee stressed the importance of sensitivity over specificity. The statement above seems to contradict this principle.	50% of referrals to a ME/CFS specialist team from a non-specialist clinician for suspected ME/CFS result in a different diagnosis other than ME/CFS. This would suggest that when clear diagnostic criteria are not applied there is a high chance of over diagnosis. As such it is important that non-specialists in ME/CS are given clear criteria to suspect ME/CFS and the committee hope the advice on how to suspect ME/CFS and the referral for the confirmation of diagnosis by a ME/CFS specialist team will reduce the rates of misdiagnosis and missed diagnosis. We note that section 2.5 of the methods manual refers to diagnostic accuracy tests and the importance of sensitivity, however the in the discussion section of Evidence review D-diagnosis there is further discussion about sensitivity and specificity in the context of the development of criteria, noting that here specificity is important. This section also includes a discussion on the heterogeneity in the study populations.
The Royal College of Psychiatrists	Evidence Review D	068	Table 7	We note the review only found one study on symptoms and signs. We were surprised by this as there are numerous studies and indeed meta-analyses that provide helpful data, although maybe did not fit the search terms  **Figure 10: Sensitivity and specificity of post-exe** **diagnosis of ME/CFS** Study TP FP FN TN Sensitivity (95% CI) Specificity (95% Jason 2011 12 35 12 47 0.50 [0.29, 0.71] 0.57 [0.46, 0.6 .	Thank you for your comment. This was the only study that matched the protocol, appendix H describe why other studies were excluded. The committee note in the discussion that each of signs and symptoms in isolation is of low predictive value but it is the combination of them that is of importance in a clinical setting and in the diagnosis of ME/CFS. In addition they note ideally evidence would have been identified that confirmed the inclusion of symptoms in the recommended diagnostic criteria. Despite this uncertainty about which of the signs and symptoms should be prioritised for diagnosis the committee agree that it is important to have a set of criteria that include the signs and symptoms

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				So PESE had a sensitivity of 50% and specificity of 0.57 which offer little support for the new diagnostic criteria. Unrefreshing sleep had a sensitivity of 0.87 and specificity of 0.31 We note that the committee chose not to be guided by this study. But it is surprising that they neither found, nor considered, the wider literature; for example Sullivan et al 2005 study of 5330 subjects from the Swedish twin registry with fatigue problems which using latent class analysis found a syndrome strongly resembling a ME/CFS like illness, but found no evidence to support a particular diagnostic value in individual symptoms - in particular post exertional malaise (doi:10.1017/S0033291705005210). As we pointed out when considering the claims of indirectness, we need to point out again under diagnosis that whilst there is no doubt that PESE is common in ME/CFS there is little evidence that it is an essential symptom (https://doi.org/10.1177/1359105318784161) Nor is there evidence of how commonly it co-occurs with unrefreshing sleep and cognitive difficulties to make a core diagnostic group. Furthermore, different groups have used different definitions of PESE and there is no agreed definition, no agreed specification of what is 'exertion', no agreed specification of the temporal relationship to exertion, and no agreed definition of what counts as a 'symptom' or as an 'exacerbation' and a wide range of patient experiences grouped together under this umbrella (https://doi.org/10.1371/journal.pone.0197811). The most recent qualitative study reported on four focus groups with 43 ME/CFS sufferers, showed just how variable PEM is. While PEM was a feature of ME/CFS, it was difficult to capture with single definition. "While three core symptoms emerged (exhaustion, cognitive difficulties, and neuromuscular complaints), participants' descriptions were notable for their	commonly agreed to be features of ME/CFS (as outlined above in the discussion of the diagnostic criteria). One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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				unique individual variations" and discussed the problems of "extensive variability" https://doi.org/10.3389/fneur.2020.01025. The College are again concerned about the scientific validity of changing a definition, and then excluding studies from review on such a weak premise. Could NICE please justify this?	
The Royal College of Psychiatrists	Evidence Review F	091	037	*"The committee are also aware from their own experience that ME/CFS is commonly misdiagnosed as depression or misunderstood to be a psychological condition, and that treatment with antidepressants is often given on the basis of these incorrect beliefs".* The College are concerned with the linking of misdiagnosis and "misunderstood to be a psychological condition". Depression is not a psychological condition. It is a serious illness that combines, as do so many disorders, physical, psychological and social factors. Although no biomarker has yet been found, like in ME/CFS, there is more replicated evidence for the role of factors such as genetics, changes in the structure and function of the brain, and neuro-immune connections than currently exists in ME/CFS, Indeed the presence of neuro-immune abnormalities back in childhood that predict the subsequent onset of adult major depression is one of the most promising lines of inquiry in research at the present, and trials of immune modulators are underway. The committee also seem unaware that antidepressants are used not just for the treatment of mood disorder, but also for sleep disorders and most of all chronic pain – both are also relevant to ME/CFS. Once again, the College notes that had a psychiatrist been on the committee, errors of this sort may have been avoided.	Thank you for your comment. After considering your comment in the context of the review the text has been edited to, 'the committee are also aware from their own experience that ME/CFS is commonly misdiagnosed as depression and that treatment with antidepressants is often given on the basis of these incorrect beliefs'. This review specifically addressed ME/CFS and the committee have noted in their overall summary for pharmacological interventions for ME/CFS that while there are not any current pharmacological cures for ME/CFS, people with ME/CFS have found some drugs when used appropriately with advice and support from health care professionals can be helpful in managing the symptoms of ME/CFS and they could be discussed on an individual basis.

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				How can this be corrected?	
The Royal College of Psychiatrists	Evidence Review G Guideline	General	CBT	Qualitative review and committee discussion - The evidence shows that CBT is clearly a safe treatment, and adverse events unusual -in keeping with experiences around the globe. But looking at the qualitative evidence it is clear that some people have not had the best experiences from CBT. In the clinical situation not that many patients will be seen in specialist settings who have had previous experience of CBT – for most it is their “first time”. But in discussion it often emerges that people might believe that they had been offered offering “CBT” but actually were not, or where patients have received other talking therapies, chiefly counselling, wrongly labelled as CBT. We know as CBT gained in popularity, and because unlike some earlier treatments, it was associated with a good evidence base overall, many therapists started calling what they did CBT, but actually did not adopt many of the procedures and standards of CBT, properly defined and delivered. The problem is not however as concerning as the issues around the misinterpretation of exercise therapies. It is rather difficult to self-prescribe CBT, or to receive well-meaning but inaccurate advice about CBT from non-professionals, friends and even family. Likewise there are no real equivalents of popular programmes aimed at the normal population such as “Couch to 5k”. nor the casual mention of the benefits of gym membership. But as with GET, we suggest that the appropriate solution to poor practice/implementation/misconceptions is not to ban a treatment but is to use education, training, quality control and quality improvement tools Will NICE make recommendations about national quality improvement programmes for both interventions?	Thank you for your comment. The committee agree that inappropriately delivered CBT, physical activity and exercise therapies can be harmful, and this is reflected in the recommendations, which include detailed information about what CBT and exercise therapies should look like for people with ME/CFS and who should deliver and oversee them. The full committee discussion of the evidence for CBT and exercise therapies and the rationale for their recommendations can be found in Evidence Review G (section 3.3). It is not within the remit of NICE to recommend national improvement programmes on specific interventions

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The Royal College of Psychiatrists	Evidence review G	323 - 336	Ex 323/36 and passim	3.3 – evidence summaries - We use the clarity of the forest plot taken from the Cochrane Review to make a general point about the presentation of results in Evidence Review G. It is very difficult indeed for the reader to understand the evidence summaries that precede the discussions of the committee. Indeed, it took us a long time to realise that a key finding – the evidence for the effectiveness of CBT on the critical outcome of fatigue - was simply missing. We are unable to check if this was a "one off" error or not. The presentational style is also sometimes misleading, for example, repeatedly including the "Null findings" for a given intervention with "Null findings" for adverse effects in the same sentences; this leads of the presumably unintended impression that both are "failures", whereas the former could be classified as a negative findings, and the latter as a positive finding. Why did they not do this?	Thank you for your comment. Thank you for pointing out that the fatigue outcomes were missing for CBT in this section of the report; this has now been corrected. To be clear, this data was missing in error from this section of the report but was still present in other sections of the report sent out for consultation, such as in the GRADE tables and forest plots. This data was presented to the committee and was considered along with the other evidence for CBT.
The Royal College of Psychiatrists	Evidence Review G	321 - 327	014	*"In general, the committee placed greater weight on moderate confidence findings than low and very low confidence findings during discussion of the evidence, although they acknowledged that some lower confidence findings reflected their own experience and should not be disregarded. The committee also acknowledged that some common themes were identified across multiple review strata and that lower confidence findings contributing to these themes could be interpreted with higher confidence when considered across studies."* We have compared and contrasted that with what the committee say about the qualitative compared with the quantitative studies – ie the clinical trials. 3.2.1 Summary of quality for review of clinical and cost effectiveness	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. The same approach was taken for the qualitative 'experiences of interventions' evidence review. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. Imprecision was determined based on clinical decision thresholds (minimally important difference (MID)) determined *a priori* by the committee. Imprecision is often a reflection of studies with small sample sizes or low number of events, which

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				Page 317 Line 23 *The majority of the evidence was of low and very low quality. The main reasons for downgrading were risk of bias, indirectness and imprecision. There was a lack of blinding in the studies due to the nature of the interventions. This, combined with the mostly subjective outcomes, resulted in a high risk of performance bias. The committee considered this an important limitation when interpreting the evidence.* 317 line 28 *Most of the comparisons only included one study. Therefore, evidence for most outcomes was based on single studies, many of which included small sample sizes. This resulted in imprecision around the point estimates.* *317 line 40 "It was therefore agreed to downgrade the evidence for population indirectness.* At no point is there anything about how some clinical trial evidence would be considered more favourably if it agreed with the committee's own views, nor that they would consider "upgrading" the findings if "common themes" were identified across "low quality" studies. Instead the comments added by the committee to the standard reporting were all clearly intended to reduce the impact of the different studies, as oppose to increase it, as happened with the qualitative studies. Indeed, they specifically point to evidence of indirectness (which is contested) and the double jeopardy of blinding and subjective outcomes, which is also contested and contrary to NICE rating procedures. They point to imprecision, but make no comment about how that might be overcome. This is clear evidence that the committee approached the clinical trial evidence in a different way to the qualitative – one needed to	results in wide confidence intervals around effect estimates resulting in uncertainty around the results. This is a limitation of the study involved and cannot be specifically addressed (see methods chapter). The committee based the recommendations on both the qualitative and quantitative evidence, as well as their own experience and knowledge of ME/CFS. Any conflicts of interests were managed in accordance with NICE's policy on declaring and managing interests for NICE advisory committees.

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				be minimised, the other the opposite. It will not be sufficient to respond that the committee made a distinction between "poor" and "very poor", because it was the committee's decision on indirectness that made that happen, and distorted the evidence. Does NICE agree that this is evidence of lack of impartiality?	
The Royal College of Psychiatrists	Evidence review G	214 - 215	Table 71	The whole summary table about counselling is based on one study mentioned above (Ward et al, 2018). Would it not be better to conclude that there were insufficient studies to provide any summary conclusions?	Thank you for your comment. Indeed, there was only one study available for counselling that met the review protocol and was included in the evidence review. Findings emerging from this study have been taken into account by the committee however, decision making was not solely based on the findings of this study. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
The Royal College of Psychiatrists	Evidence review G	020 - 021	Fulcher 1997	*"Exercise performance measure reported but not analysed: max HR, recovery HR, post-exercise blood lactate, maximal quadriceps voluntary contraction*." This is inaccurate. Fulcher and White 1997 gives all these results in table 2 of the paper, both at baseline and after treatment in both GET group and control intervention, with analysis thereof. We suggest that the review is revised to correct this please	Thank you for your comment. The committee agreed not to extract these individual physiological and biochemical outcome measures for any studies as they were not considered useful for decision-making purposes, and were not the type of outcome measures the committee intended to include as 'exercise performance measures', as supported by the examples given in the review protocol in evidence review H. The text in Evidence Review G has been updated to reflect this.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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The Royal College of Psychiatrists	Evidence Review G	005	008	*"There is no known cure for ME/CFS and non-pharmacological management strategies have been developed"* The College are concerned that the Committee have a misunderstanding of non-pharmacological treatments in general. We employ non pharmacological treatments whether or not there is a pharmacological treatment available. There is nothing unusual in using non-pharmacological treatments as first line treatments in many disorders, perhaps reserving less popular, more expensive or risky pharmacological or surgical interventions for later. Patient choice is very important here – some prefer pharmacological treatments, some don't, and we know that people generally do better when they receive the treatment they prefer – hence patient preference trials. The use of the term "cure" is also strange. Given that the committee agree that ME/CFS is a condition in which relapse and remission are common, talking about a "cure" is difficult". One can never be certain that a relapse might occur. Again this seems to talk to a narrow mind set which is rarely helpful when discussing the best approaches for any long term condition, and is not used in the rehabilitation literature. Treatment or therapy is preferred. How did the committee decide that GET/CBT were not treatments, as had been determined by their predecessors for the 2007 Guideline, but a "management strategy" before the evidence had been looked at? The committee did not appear to look for evidence that people had achieved pre-defined outcomes that would ordinarily be described as "successful treatment." The evidence is there had the committee had wanted to find it.	Thank you for your comment. The committee agree that patient choice is paramount, and this has been emphasised throughout the guideline. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. We do not rely on interpretation of data by trial authors, which includes author defined definitions of treatment success/failure, due to the risk of bias associated with this reporting, as well as the difficulty in meta-analysing outcomes where different cut-offs/thresholds have been used in different studies. We perform our own analysis on study data and determine clinical benefit or harms based on clinical decision thresholds, known as the minimally important differences (MIDs) which are determined *a priori* by the committee. Detailed information on this process can be found in the methods chapter.

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				We ask that NICE seek this evidence.	
The Royal College of Psychiatrists	Evidence review G	006	007 & table 1	The PICO characteristics of the review question was stated as "Population - Adults, children and young people who are diagnosed as having ME/CFS" The population was not adults, children and young people who are diagnosed as having ME/CFS who also have PEM. Therefore trials that recruit patients "diagnosed as having ME/CFS" should not be down-graded on the basis of not mandating PEM, since they are the exact population defined by PICO. Will the review team correct this?	Thank you for your comment. The PICO characteristics set out the population to be included in the review. As you recognised, we did not specify that study participants must have PEM in order to be included in the review, therefore trials were included if they met the inclusion criteria regardless of whether or not participants had PEM or whether or not this was reported. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Evidence review G	007	028	It is normal practice for NICE Reviews to use information gathered in any previous Cochrane Reviews. "Three potentially relevant Cochrane reviews were identified but were not included	Thank you for your comment.

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				in this review due to differences in the review protocols." The reasons given were that one Cochrane review of exercise interventions (Larun 2019) and one Cochrane review of cognitive behavioural therapy (Price 2008) did not include all critical outcomes specified in this review protocol and included study populations where not all participants had ME/CFS. (according to the Committees definition). The College thinks that these reasons are unsustainable. We have presented evidence to challenge the rating of indirectness that the panel made for the vast majority of the RCTs. The same argument clearly applies here, but with two significant additions. The Cochrane authors were aware of this issue. They did include trials with a few other participants who did not have a diagnosis of CFS/ME, but adopted the same pre-set thresholds of 90% ME/CFS as this NICE guideline has for predominant group (NICE methods review page 12 line 8), and also used subgroup analyses, which was indeed just what the NICE panel had discussed as being absent from the literature in section. The Cochrane Review would have assisted them to answer their own questions, since it did a subgroup analysis by diagnostic criteria. Even if this premise was accepted, that of indirectness, and we think that it should not have been, when it came to those trials (which was 90% of them) the end result was that trials were downgraded in quality, but not formally excluded. But why were the Cochrane reviews excluded all together? This seems inconsistent. Can NICE please explain?	Three potentially relevant Cochrane reviews were identified but were not included in this review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. **Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. **Price 2008:** This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed

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					with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. **Adams 2009:** This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full)
The Royal College of Psychiatrists	Evidence review G	007	028	Another reason given to exclude the Cochrane Reviews because they did not include all the critical outcomes agreed by the panel and listed in the Methods review. It would seem that the one missing was mortality. But the panel would have already known that no trial of any intervention in ME/CFS would have included that as a primary or secondary or any other outcome. Had they done so, the power calculations would have immediately indicated that this would have been nonsensical, not least the follow up period required to examine this outcome. The best evidence already available suggests that all cause mortality is not increased in ME/CFS, with the possible exception of suicide (Carr et al, 2019, https://doi.org/10.1017/S0033291719001065; Roberts et al, 2016, http://dx.doi.org/10.1016/S0140-6736(15)01223-4). Can NICE please explain?	Thank you for your comment. Three potentially relevant Cochrane reviews were identified but were not included in this review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. **Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity

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					levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. **Price 2008:** This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. **Adams 2009:** This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full)
The Royal College of Psychiatrists	Evidence review G	007	028	If the panel persisted in its view that mortality, or any other variable, was indeed a critical outcome, then they should do what all panels do if a Cochrane Review does not provide them with	Thank you for your comment.

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				the information they want; that is to request that the evidence team fill the gap, starting with the basic procedures such as data pooling, checking for heterogeneity and so on. This is normal practice if for example it was clear to the group that there was new evidence to review since the publication of the existing Cochrane review, as would for example have been the case for CBT. The GET review is also still on the Cochrane database, albeit in the process of revision, but again, we are not aware of any reason or precedence for why the publicly available review was excluded. Why was this not done?	Three potentially relevant Cochrane reviews were identified but were not included in this review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. As the reviews were not included we not contact the authors for updates. **Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. **Price 2008:** This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary

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					diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. **Adams 2009:** This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full)
The Royal College of Psychiatrists	Evidence Review G	007	028	The College has not previously encountered Cochrane Reviews being excluded in this way from NICE guidelines. Can NICE cite another example? It is unhelpful for clinicians to have evidence from two reputable sources pointing in opposite directions. Can NICE either justify why the committee's view should hold sway, given that it is based on reasons that appear weak, over the conclusions of Cochrane?	Thank you for your comment. Three potentially relevant Cochrane reviews were identified but were not included in this review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. **Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the

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					following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. **Price 2008:** This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. **Adams 2009:** This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full)

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

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The Royal College of Psychiatrists	Evidence Review G	007	028 and other sections	The College considers that the decision to exclude so much data has important negative consequences for patient care. First, this would have helped overcome the problem of imprecision – which is why data pooling is conducted. Second, it might have avoided for example the baffling and huge numbers of forest plots in Evidence Review H by instead giving access to a much more understandable visual representation as seen in the excluded Cochrane Review (see below). This shows the overall results of the available trials, and also confirms that there is heterogeneity. As a result they then removed the Powell trial, which was an outlier, and then found that that the central estimate was somewhat reduced when Powell was excluded (not surprising), but in most cases it didn't affect the conclusion. Some conclusions were stronger when Powell was excluded because the heterogeneity dropped and the resulting estimate became more precise (more narrow 95% CI). What is missing from this table is the latest trial, GETSET, where indirectness is not an issue.	Thank you for your comment. This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. All included studies within this Cochrane review were cross-checked for eligibility for inclusion in our review, and all were included. Data pooling to reduce imprecision is not appropriate if there is significant heterogeneity in the studies being pooled, in this case, the interventions/comparators were different. Heterogeneity in interventions or outcomes may not always result in statistical heterogeneity in meta-analysis if results happen to be similar by chance, which can produce potentially misleading pooled effect estimates with narrow confidence intervals which falsely increase confidence in a result. We only pooled studies where we considered the intervention/comparators and outcomes to be comparable. We also stratified our data by age and severity as specified in the review protocol, which further limited the number of trials that could be pooled

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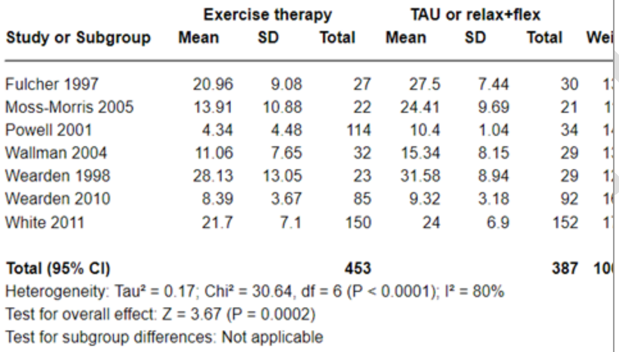
<table>
<tr><th></th><th>Exercise therapy</th><th></th><th></th><th>TAU or relax+flex</th><th></th><th></th><th></th></tr>
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<tr><td>Fulcher 1997</td><td>20.96</td><td>9.08</td><td>27</td><td>27.5</td><td>7.44</td><td>30</td><td>1</td></tr>
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<tr><td>Powell 2001</td><td>4.34</td><td>4.48</td><td>114</td><td>10.4</td><td>1.04</td><td>34</td><td>1</td></tr>
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<tr><td>Wearden 1998</td><td>28.13</td><td>13.05</td><td>23</td><td>31.58</td><td>8.94</td><td>29</td><td>1</td></tr>
<tr><td>Wearden 2010</td><td>8.39</td><td>3.67</td><td>85</td><td>9.32</td><td>3.18</td><td>92</td><td>1</td></tr>
<tr><td>White 2011</td><td>21.7</td><td>7.1</td><td>150</td><td>24</td><td>6.9</td><td>152</td><td>1</td></tr>
<tr><td>Total (95% CI)</td><td></td><td></td><td>453</td><td></td><td></td><td>387</td><td>10</td></tr>
</table>
Heterogeneity: Tau² = 0.17; Chi² = 30.64, df = 6 (P < 0.0001); I² = 80%
Test for overall effect: Z = 3.67 (P = 0.0002)
Test for subgroup differences: Not applicable

nalysis 1.1 Comparison 1: Exercise therapy versus treatment as usual, relaxation or fl

We suggest that NICE should have included the GETSET trial, and run the appropriate analyses for heterogeneity, to confirm or refute the Committees intuition.

Why did they not do this?
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<tr><td>The Royal College of Psychiatrists</td><td>Evidence Review G

(and Evidence review D)</td><td>009</td><td>Table 4</td><td>The committee could also have considered other sources of evidence, outside the narrow domain of RCTs, that might have assisted their deliberations. For example, the National Outcomes Database (NOD) included 7,041 patients assessed and treated by 29 NHS specialist CFS/ME services during the period 01/06/2010 to 31/05/2013 together with 1392 Dutch patients from the Radboud University Medical Centre Nijmegen. Symptoms of</td><td>Thank you for your comment.
The committee do not assume that people recruited to trials do not experience PEM they just don’t know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. Likewise, the committee did not assume that participant characteristics from other sources, such as those that you have</td></tr>
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				post-exertional malaise were reported in 96.5% of the UK and 87.5% of the Dutch patients (https://doi.org/10.1016/j.jpsychores.2015.12.006. The majority of downgraded or excluded trials have recruited from these centres. Unless the committee is making the implausible argument that that these trials have uniquely recruited from either the 4.5% who did not report PEM in the UK, or the 12.5% in the Netherlands – if anything given that the research teams do agree that PEM is important, if there was any bias at all, it would operate in the other direction, which when we look at the Dutch trials later, is indeed the case. Does NICE agree that this is further evidence that does not support the view of the committee on indirectness. If not, why not?	referenced, were applicable to participants recruited in trials. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Evidence Review G (and Evidence review D)	009	Table 4	The committee believes that PEM, or PESE as they labelled it, is an important symptom in ME/CFS. We agree, and this has never been in dispute But that does not mean that it automatically should be considered as a compulsory symptom, and that the apparent absence of a single symptom would then mean that the patient would not be considered as having ME/CFS and that their presence in any research study would so contaminate the evidence that it would be unsafe to use it to underpin any decisions. Yet this is clearly what has happened and the committee repeatedly emphasises the importance they put on their own opinion on this, and made no effort to even consider the possibility that there might be evidence to confirm or refute their opinion.	Thank you for your comment. As you note PEM/PESE is acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. However, the committee disagree with your view that PEM is not an essential feature of PEM, and the IOM 2015 criteria supports that. As there is no diagnostic test for ME/CFS, any evidence that exists regarding the diagnosis of ME/CFS is based on the presence of specific symptoms which differ depending on the diagnostic criteria used (which are generally consensus-based), and so there is circularity in the argument that evidence of people with ME/CFS without PEM exists. The committee considered that previous criteria, such as the Oxford Criteria and 1994 CDC criteria identify a heterogeneous population, which may or may

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Yet such evidence did exist, and at the very least calls into question their decision, yet was never looked at. The committee had noted at the start of the review, and before they briefed the evidence team on indirectness, that "the majority of the evidence was based" on the CDC 1994 as indeed it was and is. This only emphasises just how important that judgement was. We conclude by asking NICE if the committee has misdirected itself. How might this be rectified?	not include people with ME/CFS (See Evidence review D – diagnosis). The committee also emphasise that it is not the presence of this symptom in isolation, but the combination with other symptoms, particularly with the addition of PEM that are important in the diagnosis of ME/CFS. Also note term PEM will now be used in the guideline as the committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE
The Royal College of Psychiatrists	Evidence review G	013	Clark et al, 2017	"*Dichotomous reporting of continuous outcomes not extracted (improvement/deterioration of from baseline in fatigue and physical functioning scales) not extracted.*" This is an inaccurate statement since the paper gives the proportions of each intervention group which improved by a priori set thresholds for both primary outcomes (3 or more points for fatigue and 8 or more points for physical function)(table 3). Fatigue: 62 (64%) improved from baseline after guided graded exercise self-help (GES), and 45 (44%) in the control arm (X2 7.8, p = 0.005). Physical function: 44 (45%) Improved from baseline after GES, compared to 22 (22%) in the control arm (X2 12.7, p < 0,0001). We suggest that the review is revised to correct this please. Regarding deterioration, table 6 in the paper provides the numbers (%) of participants who rated their both their ME/CFS and their overall health as "much worse" or "very much worse" (deterioration) and improved ("much better" and "very much better"). Those in the GES group show no greater deterioration than those in the control group. GES was associated with a significantly larger number of participants rating their CFS and overall health as better, than the control intervention.	Thank you for your comment. To clarify, we are not saying they were not reported, but that we did not extract them. We do not rely on interpretation of data by trial authors, which includes author-defined definitions of treatment success/failure or dichotomisation of continuous outcomes, due to the risk of bias associated with this kind of reporting, as well as the difficulty in meta-analysing outcomes where different cut-offs/thresholds have been used in different studies. We perform our own analysis on study data and determine clinical benefit or harms based on clinical decision thresholds, known as the minimally important differences (MIDs) which are determined *a priori* by the committee. In this case, final values and adjusted mean differences for fatigue and physical function were also reported, which were extracted. Detailed information on this process can be found in the methods chapter. With regards to the global impression of change outcome, thank you for pointing out this omission. The global impression of change in overall health has now been added to the review.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				We suggest that the review is revised to correct this please	
The Royal College of Psychiatrists	Evidence review G	014	Clark et al, 2017	The evidence review incorrectly provides data on age: "(mean age (SD): GET 28.1(11.1); control 38.7 (12.7))." The actual figures are GET 38.1 (11.1); control 38.7 (12.7). (table 1 of the paper) We suggest that the review is revised to correct this please	Thank you for your comment. Thank you for pointing this out. This has now been corrected.
The Royal College of Psychiatrists	Evidence review G	021	Fulcher 1997	"Study reports fatigue VAS but range unclear" The range for this measure is given in a paper cited in reference 37: White et al. The validity and reliability of a fatigue syndrome that follows glandular fever. Psychol Med 1995;25:917-24. (0 = no fatigue, 100 maximum, for each of the four scales). We suggest that the review is revised to correct this please.	Thank you for your comment. The results reported in the paper were not consistent with a scale range of 0-100. Mean scores reported for the total fatigue VAS exceeded 200, and mean scores for the mental and physical subscales for fatigue VAS exceeded 100. The included studies table text has been amended to reflect this. The Chalder fatigue scale is already included in the review.
The Royal College of Psychiatrists	Evidence Review G	034	017	*""but recognises that thoughts, feelings, behaviours and physiology interact with each other "* We agree this is a good description of the assumptions of CBT	Thank you for your comment.
The Royal College of Psychiatrists	Evidence review G	038	Powell 2001	"*Serious indirectness relevant to the control group since it included an element of the intervention in that graded activity was encouraged.* But this involved only a booklet compared to a therapy in the other interventions. So, while this might conceivably be an explanation for not finding significant differences between the control and active interventions, it cannot explain what was actually found – large and significant differences in outcomes associated with the exercise interventions. This is therefore not "serious indirectness". We request a reconsideration of this judgement please	Thank you for your comment. This has been downgraded as receiving any component of the intervention is not the same as not receiving the intervention/being in a control condition. This limits our confidence about the extent to which the evidence actually provides information about the comparison examined.

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The Royal College of Psychiatrists	Evidence Review G	194	Table 64	The interpretation of the health economic results given in Table 64 is misleading. CBT had a 47% likelihood of being the most cost-effective option of all interventions in the PACE trial, not of just being cost-effective. The inclusion of GET as a comparator understandably reduced the likelihood of CBT of being most cost-effective because in some of the replications GET had a higher net benefit than CBT."	Thank you for your comment. We agree that the table under-reported the probability that CBT is cost effective. We have revised the table as follows: Probability intervention is the most cost effective (£20K/£30K threshold): SMC: 24%/8% CBT: 48%/63% APT: 3%/3% GET: 25%/27%
The Royal College of Psychiatrists	Evidence review G	202 - 007	Table 68	The range of the number of participants per study was from 9 to 43. Recruitment was from specialist care, primary care, through to advertisements. Diagnoses were self-reported, through to meeting accepted CFS or ME criteria. Participants were children, adolescents to adults. I.e. they studies were very heterogeneous. Perhaps the most important criticism to answer is the inconsistencies between the standards of quality necessary for quantitative studies, such as trials, and those standards met by these studies. The consequence is that almost all RCTs are rated "low" or "very low" in quality, whereas qualitative studies are rated as "moderate" or "low" quality. This is particularly the case when the committee lays such emphasis on qualitative studies. The College note with surprise that such concerns were only rated as "minor" in the narrative summary on pages 227-235, and these findings were rated as moderate in quality. Could NICE comment on how much reliance the committee should place on studies of such a range of provenance and methodology?	Thank you for your comment. We agree studies were heterogeneous. In line with the review protocol (see Appendix A, Evidence review H) we have reported findings for Adults and children & young people separately. Methodological limitations such as those noted about inclusion/recruitment have differently impacted the overall quality assessment of different findings depending on how much the study with such limitations contributed to the overarching theme/finding. The ME/CFS guideline committee agreed that PEM is central to the diagnosis of ME/CFS and as such any evidence without a PEM population may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to or the indirectness rating in the case of quantitative findings and in turn on the overall assessment of confidence in the findings (for qualitative findings) or the level of evidence quality (for quantitative findings). As part of this the committee

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					agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance/indirectness. See evidence review H Appendix: PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee considered that the overall results of a study were unlikely to be significantly affected by participants without PEM when the above threshold was met. Quantitative evidence quality and the assessment of confidence in qualitative evidence influenced the weight placed on findings during decision making that was also based on the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed)
The Royal College of Psychiatrists	Evidence review G	208 - 013	Table 69	There was even greater heterogeneity in these studies, with recruitment from services through to members of patient organisations. We know that the latter group are likely to contain people who do not have ME/CFS. See Brimmer et al. BMC Research Notes 2013, 6:309. http://www.biomedcentral.com/1756-0500/6/309. These authors found that a thorough clinical assessment of members of a patient support group found that only 35% actually had CFS. The College could not see much consideration given to this potential weakness. How confident are the committee that these findings apply accurately to people with diagnosed ME/CFS? How confident are the committee that these findings are not subject to a "serious risk of indirectness" because it is not clear how many have PEM?	Thank you for your comment. The ME/CFS guideline committee agreed that PEM is central to the diagnosis of ME/CFS and as such any evidence without a PEM population may not accurately represent the ME/CFS population and raises concerns about the generalisability of the findings. After considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance rating of qualitative findings they contribute to or the indirectness rating in the case of quantitative findings and in turn on the overall assessment of confidence in the findings (for qualitative findings) or the level of evidence quality (for quantitative findings). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were

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					not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance/indirectness. See evidence review H Appendix: PEM-reanalysis for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee considered that the overall results of a study were unlikely to be significantly affected by participants without PEM when the above threshold was met.
The Royal College of Psychiatrists	Evidence review G	208 - 013	Table 69	Another problem with relying on these studies is that we have no clear way of knowing what treatments patients actually received. Whether it was provided by a specialist therapist, trained in ME/CFS. Whether it was provided in a manner consistent with the 2007 NICE guidelines. See: Gladwell and colleagues (included in the NICE evidence), who showed that this was often not the case. These authors concluded: "*The negative themes may help explain the negative outcomes from rehabilitation reported by previous patient surveys. The negative themes indicate rehabilitation processes which contradict the NICE (National Institute for Health and Clinical Excellence) Guideline advice regarding GET, indicating that some clinical encounters were not implementing these. These findings suggest areas for improving therapist training, and for developing quality criteria for rehabilitation in CFS/ME*." (Gladwell PW, et al, 2014, https://doi.org/10.3109/09638288.2013.797508). The latter suggestion is what the current guideline committee should do – develop quality criteria for these rehabilitation therapies, rather than ban them. The College noted minimal discussion of this potential weakness in some of these qualitative studies. How confident is the committee in relying on this evidence, when it is likely that a significant number of people in these studies did not receive either CBT or GET in ways that they should have, and as described previously by NICE?	Thank you for your comment. Recommendations in NICE guidelines are developed using a range of evidence . In addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Within this framework the committee considered quantitative evidence as well as peoples' qualitative experience of interventions together with their clinical experience from working with people with ME/CFS.

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					It is not always possible to gain sufficient insight on how interventions were received in the studies included in the evidence and the committee acknowledges there are limitations in the evidence and these have been accounted for in the assessment of confidence in the findings. The current evidence was not the only source of information the committee considered when making recommendations. The committee agree there is a context within which interventions should be applied and were able to use their clinical expertise to agree on the content, approach and delivery of interventions included in the recommendations. For example, recommendations specify that CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS, and under the clinical supervision of someone with expertise in CBT for ME/CFS. Specific recommendation about the content of CBT for ME/CFS have also been made. The same applies to programmes involving physical activity or exercise.
The Royal College of Psychiatrists	Evidence Review G	197	Table 66	The interpretation of the health economic results given in Table 66 is misleading. GET had a 25% likelihood of being the most cost-effective option of all the interventions in the PACE trial, not of just being cost-effective. The inclusion of CBT as a comparator needs to be taken into account	Thank you. We agree that the table under-reported the probability that GET is cost effective. We have revised the table as follows: Probability intervention is the most cost effective (£20K/£30K threshold): SMC: 24%/8% CBT: 48%/63% APT: 3%/3% GET: 25%/27%
The Royal College of Psychiatrists	Evidence Review G	214 onwards 320 onwards		Qualitative research summary and committee discussion - Sadly offering CBT in the context of ME/CFS is interpreted by some as saying that proves that the person is not really ill, ME/CFS is imaginary, all in the mind and so on. We know from our long experience, and this is echoed in some of the qualitative	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage

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				comments in the Review, that there are still health professionals, friends and family who do still believe this. We hope the review will give a loud and clear message that this is untrue. It has the opportunity to do so, which will undoubtedly be of comfort and reassurance to many who are troubled by this. A recent report noted that one of the reasons for the controversies that beset this field is that some sufferers do find these treatments stigmatising https://www.cjr.org/special_report/the-lancet-covid-19-medical-studies-politics.php. As psychologists, psychiatrists and mental health professionals we need no reminding of the pervasive effects of stigma in all walks of life – and this Review could be an ideal opportunity for combatting that stigma, rather than perpetuating it. But whatever actions NICE take, this surely cannot be a reason for misrepresenting CBT, or marginalising or distorting what it can achieve Can NICE please comment?	their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Royal College of Psychiatrists	Evidence review G	214	Table 70	"*Some perceived CBT as controlling, patronising and a form of brainwashing.*" There was only one reference for this finding: Ward et al The experiences of counselling for persons with ME. Counselling and Psychotherapy Research. 2008. https://doi.org/10.1080/14733140801972760 This was a study of 25 members of two patient organisations who had received "any type of counselling". The paper described: "It is difficult to be precise about who had received which approach to counselling, since many participants were unclear about the theoretical orientation of the counsellor they had seen. From the material, it seems that participants had experienced CBT, person centred, psychodynamic and	Thank you for your comment. Indeed, there was only one study available that met the review protocol that this emerged from. Findings from this study, along with the study's methodological limitations, have been taken into account by the committee however, decision making was not solely based on these findings. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of

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				integrative/eclectic approaches." Although Ward et al go on to say: "Eight participants were clear that they had received CBT, and a further four described CBT techniques in some detail. This seems to be the predominant single approach experienced by the participants." The evidence that counselling was brain-washing or patronising was quotes given by two patients and a statement from the authors that "some participants found these kinds of suggestions very patronising and negative." And "certain styles of counselling were perceived as controlling, patronising and a form of brainwashing. These perceptions generally related to what the participants understood as CBT." Ward et al suggest that there may have been a selection bias: "It is possible that the lack of fully recovered participants in our sample reflect the recruitment strategy. All of the participants were recruited via the ME Association and the Action for ME user group. As a consequence, it is possible that most participants would have had a long history with unremitting symptoms". A further and opposite selection bias is that as the ME Association has been campaigning for some time for the withdrawal of CBT and GET, it would not be a natural haven for those who have found CBT beneficial, and this is what our members do hear from patients attending for follow up who have done well on CBT. Much the same is true for social media. Was this sufficient evidence to allow the committee to reliably conclude that CBT, as recommended by NICE, was found to be brain-washing or patronising by patients in general?	the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). As a result the present findings from the individual study available were considered along with all the aforementioned factors together with the committee's clinical experience and conclusions regarding CBT as well as the recommendations made were not determined by this finding. The committee agreed on the benefit of CBT for the management of symptoms of ME/CFS and a recommendation to offer CBT to people with ME/CFS has been made to ensure that this intervention in available to all people with ME/CFS.
The Royal College of Psychiatrists	Evidence review G	214	Table 70	We describe this in depth because it illustrates a central problem in the qualitative research – the issue of selection bias. NICE is well aware that surveys of patient groups come with their own methodological problems. As a generality they are more likely to include those who remain unwell than those who have recovered - and this is acknowledged in this review, where evidence summaries do point out that "recruitment through a single ME	Thank you for your comment. We agree there are limitations in qualitative evidence that may limit the extent to which conclusions can be drawn for the population of interest. We have carefully considered the information available on the survey methodologies to quality assess the surveys and bring methodological shortcomings such as potential selection bias to the committee's attention when discussing the evidence. Such

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				charity potentially meaning participants were more likely to be those who had not improved/recovered", although it is hard to see where this influenced the Committee discussions. There are also more specific issues as well. ME/CFS has become a deeply polarised subject, as NICE will be aware. We know from our own experiences in ME/CFS services that those who have done well from CBT/GET are not always well received by some patient groups. Many have been attacked on social media, and often told that they could not have had ME/CFS. We often advise them against going on social media for that reason. These voices will be rarely heard in surveys of some patient organisations. We have only recently become aware of the work of Recovery Norway, which seeks to redress some of this imbalance, and gives a space for much more positive views of rehabilitation and recovery from ME/CFS. All are people who have been diagnosed with ME/CFS, and have recovered. The site has been active for 2 years, and already has 100 stories, which half which have been translated into English https://www.recoverynorway.org/ . As no similar resource is available in the UK, and we cannot think of any reason why these stories should be specific only to Norway. We therefore ask NICE to take account of these perspectives	limitations in the studies have been accounted for in the assessment of methodological concerns at the study level (specified in the Qualitative evidence tables in Appendix D, Evidence review H) and in the assessment of confidence in each review finding they contribute to. The level of confidence in each review finding which has been partially based on such methodological concerns, along with concerns over coherence, relevance of the study populations, interventions received, the setting and the adequacy of information there is to support the finding, is taken into account by the committee when discussing the review findings as it is evident throughout the discussion sections of the evidence reviews. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). As a result survey results have been considered together with many different sources of evidence and conclusions regarding CBT and GET as well as the recommendations made have not been determined by survey results.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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The Royal College of Psychiatrists	Evidence review G	215	Table 72	Summary findings mixed up GET with other exercise interventions, when the previous NICE guidelines had only recommended GET, and the best evidence of efficacy is for GET. Reference 14 (Brouwers, 2002) was a trial of a nutritional supplement, not a qualitative study of an exercise intervention. Reference 21 (Collinge 1998) was a trial of meditation and qui gong, with no qualitative methods. Reference 38 (Janse) was a trial of CBT, not an exercise intervention. Reference 54 (Moss-Morris) was a trial without qualitative methods. Reference 61 (O'Dowd) was a trial of CBT. Reference 77 (Rimes) was a trial of CBT. The fact that only 2 of the 8 citations were relevant to this table diminishes the College's confidence in these findings considerably.	Thank you for your comment. We have stratified the qualitative evidence by intervention type in line with what had been pre-specified in the review protocol (see Appendix A- Review protocols, Evidence review H). Nevertheless, based on the similarity of experiences emerging from the different studies relating to exercise interventions, the majority of themes relevant to exercise interventions related to GET with studies on GET such as Cheshire 2020 and Gladwell 2014 often individually contributing to different findings (such as 'competing commitments', 'comorbid conditions', conflict in beliefs', 'overall approach', knowledge and understanding') or synthesised together under the same theme with no further studies contributing (such as in 'baseline activities and false starts'). Despite some findings from different exercise interventions summarised together under the same theme, the committee discussed GET in detail separately as it has been reflected in the Committee's discussion and interpretation of the evidence section in Evidence review G. Also in line with NICE methods (see Developing NICE guidelines: The manual) Findings from the quantitative evidence have been summarised on a comparison basis meaning that only studies looking at GET have been summarised in the same table. Apart from the findings emerging from both the qualitative and the quantitative evidence, the committee utilised their clinical experience to inform decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Brouwers 2002 has been included in the polynutrient supplement versus placebo comparison in the quantitative evidence, not in the exercise interventions. Similarly Collinge 1998 has been included in the Mindfulness and medical Qigong versus Usual

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					care in the quantitative evidence; Janse in the evidence for CBT; Moss Morris in the quantitative evidence; Rimes in Mindfulness based cognitive therapy and O'dowd in CBT. We appreciate the confusion regarding the references has resulted from previous errors in the reference numbers in the review. Thank you for pointing out the incorrect references and apologies for the confusion this may have cause. These have now been corrected.
The Royal College of Psychiatrists	Evidence Review G	222	020	We have been aware for over 20 years that many ME/CFS patients have not had good experiences in their encounters with the health services before they reach specialist ME/CFS services, including those in which our members work. (Deale 2001 https://pubmed.ncbi.nlm.nih.gov/11352411/). A core features of CBT, particular at the start, is to help overcome the impact of stigma or the ignorance of others. One of the most important parts of CBT is that the therapists are trained to acknowledge and empathise with patients and validate their symptoms and negative experiences with other health professionals. This is acknowledged in the Qualitative Evidence summary (Review G, 222, 20) "Treatment was perceived as a source of validation. CBT helped people to feel understood and to reaffirm that their suffering is real and recognised. CBT provided a non-judgemental environment for people to express themselves. This should be further emphasised as a particular important feature of CBT in the management of ME/CFS, and should be specifically highlighted to remove one of the misunderstandings of CBT that is mentioned elsewhere in the review	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Royal College of Psychiatrists	Evidence Review G	226	003	We note that in the summary of the qualitative evidence on CBT the word treatment is mentioned 17 times, but only once in a negative context. Has the Committee overestimated the degree of objection to CBT as a treatment? It is not something that our members report hearing very often if at all. More often people simply ask whether it might help them, and our members	Thank you for your comment. From the qualitative evidence and the committee's own experience, they are aware of instances where some interventions, including CBT, are being misrepresented to people with ME/CFS and promoted as a cure for ME/CFS. Therefore, the committee agreed it was important to explicitly state that that

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				normally response "yes, it might, and also think unlikely to do any harm" Would NICE comment please?	there is no current cure (previously worded as treatment or cure – see below) for ME/CFS. The committee recognised that CBT can be helpful for some people, and this is reflected in the recommendations. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Royal College of Psychiatrists	Evidence Review G	316 onwards		Committee deliberations 3.1 onwards - Overall we consider that the committee lacked appropriate knowledge of non-pharmacological trails. It is in retrospect disappointing that they had no members with the requisite experience who could have guided them through these issues or that they did not take expert evidence from anyone with the requisite non-pharmacological trials experience. Might NICE suggest how this deficiency will be corrected?	Thank you for your comment. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership reflects the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence . When developing

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					this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). In recognition that the views of people with ME/CFS who had experienced the interventions was important, this review was done with an accompanying call for evidence which allowed registered stakeholders to submit information relating to the review question. Evidence submitted within this call for evidence was assessed for inclusion in the evidence review in addition to the evidence identified in the systematic searches following the same process of assessment against the review protocol. Experiences of interventions identified through the call for evidence have also been included in the Evidence review to help the committee draw conclusions about people's experiences of

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					non-pharmacological interventions along with the range of evidence that underpinned decision making.
The Royal College of Psychiatrists	Evidence Review G Guideline	316 065	021 11	The contrast with other draft Guidelines, for example the Chronic Pain guidelines soon to be published, could not be more stark. Chronic pain overlaps considerably with ME/CFS as the committee acknowledge on numerous occasions, and refer both patients and practitioners to the NICE Pain Guidelines, soon to include the Chronic Pain Guideline. But the ME/CFS and Chronic Pain Guidelines are very different. For example in this review (https://www.nice.org.uk/guidance/gid-ng10069/documents/evidence-review) , the Chronic Pain Committee examined what were the barriers to successful management of chronic pain. This question is equally relevant to the ME/CFS review – what are the barriers to successful management of ME/CFS. But from then on the two paths could not be more different, and the reviews seem almost to come from different planets. The Chronic Pain review in its opening sentence states that these barriers are biological, psychological and social. Each are then considered in turn and in similar detail from the start to the finish. None are ignored or overlooked. The list of contents (page 4) is explicit that biological, psychological and social are going to get equal weight. The first line of the ME/CFS Recommendations opens with a clear statement that this is a "chronic medical condition" even if the cause and pathophysiology is unknown. And it is clear from the rest of the review that, even if they don't know what it is, the committee are certain what it isn't – anything psychological or social. So rather than remaining balanced as the Chronic Pain committee did, and acknowledging that all three of the	Thank you for your comment. The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account. Guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. In addition to this, as with all NICE guidelines, recommendations were developed using a range of evidence . When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions, the committee

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				aforementioned factors could be contributing to, for example, barriers to recovery, and endorsing treatment modalities that address all these areas, the ME/CFS committee seemed keen to do the reverse. It is difficult on reading the documentation from start to finish to come to any other conclusion. Likewise ,we note that a number of major decisions taken by the committee, not to mention more minor errors and inaccuracies, always seem to go in the same direction, namely reducing the importance given to psychological issues and/or psychological or behavioural treatments. Will NICE please look at the Chronic Pain Guidelines, note the major discrepancies, and indicate how they intend to respond to these?	used its judgment to decide what the evidence means in the context of the review topic, and their clinical experiences with patients, particularly in areas where evidence has lacked. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
The Royal College of Psychiatrists	Evidence review G	316	029	The College notes with concern that *"The committee acknowledged the lack of existing objective outcome measures of effectiveness of interventions for ME/CFS and the limitations of self-reported measures (see Professor Edwards expert testimony – Appendix 3:"* (see also 3,2,1, lines 21 onwards) "*There was a lack of blinding in the studies due to the nature of the interventions. This, combined with the mostly subjective outcomes, resulted in a high risk of performance bias. The committee considered this an important limitation when interpreting the evidence"* This is a misconception about ME/ CFS. Our key message is that it is the self-reported measures that most closely correlate to the experiences of the patient – indeed, if there was a move to "objective" measures we believe that his would be a major step backwards, and the losers would undoubtedly be the patients. It would favour the "your tests are normal, there is nothing wrong with you" approach, which accounts for so many experiences of disbelief reported by ME/CFS sufferers and a principal source of justified anger commented on in the Guidelines.	Thank you for your comment. The risk of bias for subjective outcomes in unblinded studies needs to be acknowledged, however, this doesn't mean these outcomes shouldn't be assessed or aren't important. The committee considered the results of both objective and subjective outcomes, as well as qualitative evidence, when making their recommendations. The committee noted that there is considerable controversy over the outcome measures used in trials of treatments for ME/CFS and managing symptoms. Inconsistency in outcomes used and concerns over the validity of some outcome measures in an ME/CFS population makes it difficult to combine and compare results from different trials, limiting the ability to draw conclusions on the clinical and cost effectiveness of interventions. The committee made a recommendation for research on core outcome sets to enable the direct comparison of treatments for ME/CFS and symptom management and shape and optimise ME/CFS trial design. See the research recommendations in report X for more details.

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				As with many other conditions it is the self-reported outcomes that are the primary expression of the illness; so called "objective" measures often have very little relationship to the key experiences of the sufferer. This is clearly true for all chronic pain conditions and all disorders characterised by fatigue, including for example clinical trials treating fatigue after stroke or in the context of multiple sclerosis. The committee rightly remarks that cognitive difficulties are a key experience in ME/CFS. However standard neuropsychological testing has been known for many years to be largely normal. 30 years of neuropsychological research confirms that these cognitive symptoms are largely unrelated to deficits on testing, (Rascouli et al Neuropsychological Dysfunction in Chronic Fatigue Syndrome and the Relation Between Objective and Subjective Findings Neuropsychology 2019: 33; 658-660). There are discrepancies between self-reported experiences of pain and the "objective" assessment of pressure pain thresholds doi: 10.1515/sjpain-2020-0031. Likewise there are discrepancies between subjective symptoms of immune alterations (chills, tender lymph nodes, etc) as well as subjective symptoms of autonomic alterations (orthostatic intolerance, palpitations, etc.), and objective markers of immune and autonomic alterations, respectively. These results were similar comparing the CDC 1994 case definition, which the committee do not like, with the Canadian 2003 criteria http://pubmed.ncbi.nlm.nih.gov/32892183 Again, the direction of travel was always the same, the self reported symptoms did not correlate with the "objective" symptoms. The same is true of exercise studies. A very long literature confirms that there is a discrepancy between the patient experience and the results of standard exercise testing. What is at issue is not exercise performance on a treadmill – but the	With regards to your comment on exercise performance measures, the committee agree that subjective outcome measures such as perceived exertion could be useful. Data on perceived exertion (generally reported as the Borg Scale) have now been extracted and included in the review.

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				extreme and unprecedented effort that it requires and the consequences they will suffer later. See Barhorst et al. 2020 Elevated Perceived Exertion in People with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Fibromyalgia https://doi.org/10.1249/mss.0000000000002421 Across medicine we find the same – so for example the Heart and Soul study looked at this and found that physiological measures, in a cardiac condition which had plentiful biomarkers, did not predict patient related outcomes, whereas subjective measures of mood did. This is now widely accepted and part of the reason that people are moving away in general medicine from exclusive reliance on objective outcome measures and realising that PROMS are also essential. https://pubmed.ncbi.nlm.nih.gov/12851276/ So self-reported outcome measures, using reliable scales, are not a poor alternative to objective measures, but instead bring the trial closer to the patient experience. Even in fatigue secondary to known neurological conditions. ME/CFS is one of the many conditions in which Patient Recorded Outcomes (PROMS) are the endpoints of choice. Some say that the solution is a better test, but there is no sign of that at the moment. Any single biomarker is most unlikely anyway to be found in all current ME/CFS sufferers, leaving many even more out "In the cold". A better solution is to believe the patient in the first place. So are NICE concerned about turning back the clock to the period before PROMS become widely accepted? If this view is accepted might NICE please tell us how many other Guidelines they expect to have revisit?	

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The Royal College of Psychiatrists	Evidence review G	317	031 - 041	"*The committee agreed that a population diagnosed with such criteria may not accurately represent the ME/CFS population and that people experiencing PEM/PESE are likely to respond differently to treatment than those who do not experience PEM/PESE and this raised concerns over the generalisability of findings to the ME/CFS population.*" The PICO question at the beginning of this review defined the population as patients diagnosed as having ME/CFS, not only those who also had PEM. Since a minority of patients diagnosed with ME/CFS do not have PEM recorded (see evidence from CBT and GET trials) downgrading trials recruiting such patients will diminish generalisability, not increase it. And there is no evidence to support the second assertion – that having the symptom of PESE makes you less likely to respond to CBT or GET. There is clear evidence to the contrary. Could NICE correct this please?	Thank you for your comment. The committee considered that PEM/PESE was a key feature of ME/CFS. As there is no diagnostic test for ME/CFS any diagnosis relies on the presence of a specific set of symptoms, and this differs depending on which diagnostic criteria is used. Therefore, trials using different criteria, particularly those without PEM as a compulsory feature, may identify heterogeneous populations who may or may not have ME/CFS. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. Few studies reported the percentage of participants with PEM. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. Downgrading trials for indirectness acknowledge the difficulty in interpreting the evidence and the uncertainty regarding the study population and therefore the possibility of reduced generalisability of the evidence; it does not cause the generalisability to be reduced. Also note term PEM will now be used in the guideline as the committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE

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The Royal College of Psychiatrists	Evidence Review G	317	042	The Committee had noted that *""Evidence was not stratified by diagnostic criteria used, so theoretically, studies including potentially different populations could have been combined"* But there was nothing theoretical about this. It had been done and was available to the committee. The largest trial (White et al, 2011) did a sensitivity analysis, looking specifically at the London criteria, included in the trial protocol and which mandated PEM. There was no significant difference in outcomes between CDC, Oxford and the London Criteria. The trial also analysed the impact of all four interventions on PEM. GET and CBT improved PEM more than either pacing therapy or standard medical care (Table 6 , Main paper, Figure 3 Appendix, http://dx.doi.org/10.1016/S0140-6736(11)60096-2 This contradicts the suggestion of the committee that heterogeneity in the presence of PEM, or to be more accurate the recording of PEM, might lead to a systematic bias over estimating the effectiveness of GET in "true" ME/CFS, or alternatively on the symptom of PEM. Why was this not taken into account by the committee? We do not think it is acceptable to respond that this was because the committee thought that the trial was of very poor quality, because that is a tautology. This is the evidence that confirms that the trial was not of very poor quality, and that the proper way to have dealt with this was to consider this evidence before instructing that review team to downgrade this and all the other trials on evidence of indirectness. We contend that a Committee that remained in equipoise and had not made up its mind without the evidence would then have	Thank you for your comment. This statement refers to the fact that we did not undertake any analyses stratified by diagnostic criteria, not whether or not other studies had performed such analyses. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *London criteria* The London Criteria as used in the PACE trial ('PACE trial protocol: Final version 5.0, 01.02.2006 p188) does not include post exertional malaise. On the basis of the written criteria used to assess participants in the PACE trial the committee could not establish that participants experienced post exertional malaise.

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				reconsidered its initial concerns on indirectness, which it had admitted in discussion were an intuition, not a fact, and changed their mind.	
The Royal College of Psychiatrists	Evidence review G	321	036 - 037 041 - 044	*"Most of the evidence showed no clinical difference between self-management strategies and any of the comparison groups (usual care or relaxation)."* "*Fatigue (as measured on the fatigue severity scale) showed no clinical difference in the evidence compared to usual care in a population of mixed severity and a benefit for self-management strategies in one study with a population of people with severe ME/CFS. "* In the face of little or no evidence for benefit for self-management, why does the draft guidance recommend such an approach? The opinion of the committee and patient surveys are not the same strength of evidence as that available from RCTs. Could NICE correct this please?	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Although the quantitative evidence identified was limited and no evidence was identified on people's experiences of self-management interventions in the qualitative review of experiences of interventions, evidence identified for other interventions that encouraged self-management techniques, showed that people appeared to value and benefit from this type of support. After considering the evidence identified for self-management, as well as the lack of information and support people with ME/CFS report in managing their symptoms emerging from Evidence review A and the multiplicity of the

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					abovementioned factors and their clinical experience, the committee agreed the evidence was unclear but recognised the benefits of self-management strategies for people with ME/CFS and the importance of having access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (see Evidence review G for the committee discussion on self-management strategies). The recommendations made reflect this.
The Royal College of Psychiatrists	Evidence Review G	321	Committee discussion 3.3 Methods Review, 20, line 8	The GETSET trial, which used the 2007 NICE criteria (by definition not available earlier) and which did have PEM as a mandatory criteria, showed a benefit of guided self-help based on the principles of GET http://dx.doi.org/10.1016/S0140-6736 (16)32589-2. This finding contradicts the suggestion of the committee that heterogeneity in the presence of PEM, or to be more accurate the recording of PEM, might lead to a systematic bias over estimating the effectiveness of GET in "true" ME/CFS. Does NICE agree that this is further evidence that the concerns on indirectness were misplaced?	Thank you for your comment. The committee consider PEM to be a key feature of ME/CFS and that people with PEM may reaction differently to interventions compared to people without PEM. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. The percentage of participants with PEM was rarely reported in trials. A subgroup analysis has been performed, which examines results from trials where ≥ 95% of participants had PEM separately (including the GETSET trial) to trials where <95% of

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					study participants had PEM or this was unclear (Moss-Morris 2005 and PACE trial). Due to the small amount of evidence available, the low to very low quality of the evidence the committee did not make any changes to their recommendations as a result. See evidence review H appendices F and G for full details on the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Evidence review G	322	012 - 015	"*The committee considered why the evidence showed no difference between adaptive pacing therapy and usual care. It was suggested that a possible explanation was that the extra information in the adaptive pacing group was beneficial but negated by the extra effort it took to take part.*" This is but a suggestion, and there is no evidence to support it since 85% of those participants who received adaptive pacing therapy in the PACE trial were satisfied with it. Therapy sessions were available by telephone if a participant felt unable to attend hospital. Information alone has very weak evidence as an intervention in long-term conditions. Could NICE comment please?	Thank you for your comment. The committee considered if there could be plausible reasons why the adaptive pacing intervention did not appear to be particularly effective compared to the specialist medical care arm. They noted that the specialist medical care arm included aspects of the intervention (i.e. both arms received some degree of an adaptive pacing) and they thought it was possible that this led to an underestimation of the effect of adaptive pacing as an intervention. However, this is just one possible explanation the committee considered when looking at the evidence.
The Royal College of Psychiatrists	Evidence review G	322	017 - 020	*"In addition, the definition of specialist medical care in the trial was considered by the committee to include elements of pacing, such as a patient leaflet which included avoiding extremes of activity, which may have led to an underestimation of the effect of the intervention."* The patient leaflet was received by all participants in this trial, including those who received adaptive pacing therapy, so is unlikely to explain why up to 15 sessions of therapist delivered APT + specialist medical care had no more benefit than specialist medical care alone. Providing information alone has be shown to	Thank you for your comment. The committee considered if there could be plausible reasons why the adaptive pacing intervention did not appear to be particularly effective compared to the specialist medical care arm. They noted that the specialist medical care arm included aspects of the intervention (i.e. both arms received some degree of an adaptive pacing) and they thought it was possible that this led to an underestimation of the effect of adaptive pacing as an intervention. However, this is just one possible explanation the committee considered when looking at the evidence.

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				have little efficacy as an intervention for patients with long-term health conditions. Could NICE comment please?	
The Royal College of Psychiatrists	Evidence review G	322	015 - 016	"*Some committee members felt that the adaptive pacing therapy intervention trialled encouraged an increase in activity and therefore was not a true 'pacing' intervention.*" Adaptive pacing therapy was based on the principles of pacing, as described by Jason, Pesek, and colleagues (https://doi.org/10.1300/J137v03n01_04) based on the energy envelope theory, and was supported and co-designed by the patient charity Action for ME. So it was designed to be as consistent with pacing as it was possible to be. Patients were only encouraged to do more "as able", and to do less if they became symptomatic. If it was more of an incremental activity programme, such as CBT or GET, then one would have to explain why it did not show the benefits of these two comparison treatments (White et al, 2011, cited above). Could NICE comment please?	Thank you for your comment. The committee discussed the use of the term pacing, including adaptive pacing ,and agreed that pacing means something different to different people with many different versions in use and it was a confusing term to use. We note that in PACE ,*a standardised pacing therapy was produced in collaboration with Action for ME and Professor Cox, it was called 'adaptive pacing therapy' (APT)to convey the main aim of the therapy - to enable the patient to optimally adapt to the illness'*. Some but not all committee members interpreted the description of adaptive pacing in PACE as encouraging increased activity. They considered this could be one reason why the adaptive pacing intervention did not appear to be effective when compared to the specialist medical care arm. This committee note this was only one part of the range of evidence considered in the decision making for the energy management and physical activity recommendations.
The Royal College of Psychiatrists	Evidence Review G	323	023 (missing)	The College are very concerned to note that in the summary of the CBT versus usual care findings, the outcome of fatigue is missing. We do not know if this meant that the results of these trials were not presented to the committee, but are sure they will not have been available to anyone taking part in the consultation. What has been dropped? Looking at the Forest Plots we can see that that these trials all favoured CBT. 7 of them were downgraded for imprecision but one of these was wrongly graded.	Thank you for your comments. *Fatigue outcomes* Thank you for pointing out that the fatigue outcomes were missing from this section of the report; this has now been corrected. To be clear, this data was missing in error from this section of the report but was still present in other sections of the report sent out for consultation, such as in the GRADE tables and forest plots. This data was presented to the committee and was considered along with the other evidence for CBT.

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				- Sharpe et al favours CBT - Three Dutch trials, combined with no evidence of heterogeneity favours CBT - Wilborg Favours CBT - Janise, Favours CBT (no downgrading for imprecision) - O' Dowd Favours CBT - White 2011 Favours CBT However, the White 2011 data clearly comes from the 135 week follow up. The College are concerned that this is greatly misleading, since the trial had ended at its predetermined end point, 52 weeks, after which because of the ethical approval all those who wished were able to obtain any treatment that they had not received. Many did so, more choosing CBT or GET than pacing. So to analyse by initial assignment at randomization some 18months after the end of the trial, during which period large numbers had now received a non-randomly chosen other treatment, makes absolutely no sense at all, and it clearly misleading and inappropriate. The analysis at 135 weeks also was downgraded because of imprecision, hardly surprising given the length of time. But the analyses performed on those measures that were not included at the 135 week mark do not show imprecision, again hardly surprising but potentially very important. We would recommend that NICE reinstate the fatigue data for CBT versus usual care. Second, we submit it should carry out data pooling on more than just three trials, and see what effect that has, and present the data in the same format as for the Wilborg trials. Third it must use the correct comparison for White et al, 2011 - the 52 week data. We anticipate that will also change the GRADE assignment. At the same time we have also	_Indirectness. imprecision & GRADE_ Three different fatigue scales were assessed in studies of CBT vs usual care: Chalder Fatigue scale (1 study each for web/written, individual face-to-face, and group-based CBT); Checklist Individual Strength (3 studies for web/written, and 1 study for group-based CBT); and a 0-10 fatigue scale (1 study for individual face-to-face CBT). This results in a total of 6 different fatigue outcomes assessed taking into account the different treatment modalities and different scales used, across 7 studies. We have checked the imprecision ratings for these outcomes for errors these outcomes and did not find any. Imprecision is determined by assessing the width of the confidence intervals around an effect estimate in relation to a clinical decision threshold, the minimally important difference (MID), determined a priori by the committee. Results are often imprecise when studies include relatively few patients and few events and thus have a wide confidence interval around the estimate of the effect, and this results in uncertainty about the results. Indirectness largely depends on the similarity/relevance of the research study to the review protocol, and is considered in relation to the study population, interventions, and outcomes assessed. The committee consider PEM to be an essential feature for a diagnosis of ME/CFS, and this is supported by the IOM 2015 criteria. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. Initially trials had been downgraded for indirectness if the diagnostic criteria used did not include PEM as a compulsory

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				asked for a review of the decision to regrade all the trials that were considered in the comparison of CBT versus usual care. Could NICE please consider how to present the missing fatigue data and the new grading would have influenced the decisions taken at the time by the committee?	feature, but after considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. The percentage of participants with PEM were not reported for the Sharpe 1996, Knoop 2008, Tummers 2012, Wiborg 2015, and O'Dowd 2006 studies, therefore these studies remained downgraded for population indirectness. While the percentage of participants with PEM in the Janse 2018 study (90.4%) and PACE trial (84.2%) were reported, these were both below the 95% threshold determined by the committee, and these studies also remained downgraded for population indirectness. The overall GRADE quality rating for most of these outcomes was 'very low', with the exception of Checklist Individual Strength in web/written CBT, which was 'low'. We have checked these ratings for errors and could not find any. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *Long-term follow-up* Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes.

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					All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline. *Data pooling*

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					CBT studies were analysed separately based on the delivery method (web/written, group-based, individual face-to-face), as these were considered to be distinctly different interventions
The Royal College of Psychiatrists	Evidence review G	323	027	*- none of the modes of delivery showed any more overall benefit compared to other modes.* This question has not been adequately tested. Only 2 non-inferiority trials have been performed comparing individual CBT versus stepped care (minimal intervention plus individual CBT if needed). This is not a comparison of modes. Please correct the text.	Thank you for your comment. We did not review evidence comparing different modes of intervention delivery and therefore there was a lack of evidence to allow us to draw conclusions about the benefit of any particular mode of delivery over another. This has now been clarified in the referenced text in Evidence review G.
The Royal College of Psychiatrists	Evidence Review G	323	029	*Most of the evidence showed no clinical difference compared to usual care or waiting list for quality of life, cognitive function, physical function, psychological status, pain and sleep quality.* Again, because of the absence of fatigue, this section is now very distorted. Almost all studies have fatigue as primary outcome and level of physical functioning and level of disability as secondary outcomes. Meta-analysis shows a positive effect on these outcomes. Some studies looked at other outcomes. In the 7 Dutch trials positive effects have been reported on cognitive functioning (Knoop et al, 2008); Pain (knoop et al, 2008), sleep quality (Stulemeijer et al, 2005), and psychological distress (Prins, 2001; Knoop, 2008, Tummers 2012, Wiborg 2015).	Thank you for your comment. *Fatigue outcomes* Thank you for pointing out that the fatigue outcomes were missing from this section of the report; this has now been corrected. To be clear, this data was missing in error from this section of the report but was still present in other sections of the report sent out for consultation, such as in the GRADE tables and forest plots. This data was presented to the committee and was considered along with the other evidence for CBT. *Other outcomes* Thank you for your comment. All available outcomes from Knoop 2008 have been extracted. Results from the Brief symptom inventory used to measure psychological distress have also been extracted in Evidence review G under the protocol outcome named psychological status. The outcome of unrefreshing sleep available in Stulemeier 2005 does not match protocol outcome of sleep quality as the study did not use a validated scale to measure it. Prins 2001 had a population which included people with idiopathic chronic fatigue (7% of the study population), and

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					results were not reported separately for those diagnosed with ME/CFS, therefore this study was excluded.
The Royal College of Psychiatrists	Evidence review G	324	005	*Fatigue: no difference (relaxation (moderate population), adaptive pacing therapy, 5 graded exercise therapy, psychoeducation/pacing, counselling) and benefit 6 (education and support, graded exercise therapy, cognitive therapy)* This needs to be revised because the wrong outcome period is being used. There was a clear difference between CBT and adaptive pacing therapy at the 52 weeks, the trial primary endpoint. It makes no sense to use 135 weeks, when many who were initially randomised to APT had now received CBT. The more appropriate conclusion is to note that the benefits of CBT had persisted to 135 weeks. For the rest of this section we cannot unravel which trials are being included where, and which are being combined or not. This section and the one above needs to be revised so it is clear to the reader which trials are being included in which comparisons. Without that information it is impossible to assess. We feel that at least some of the comparisons do not appear correct, but it is very difficult to understand in the way that it is presented. Might this data presentation be made clearer please?	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. . For outcomes where long-term follow-up was available, this data was preferentially extracted in line with what had been prespecified in the review protocol, as this was the longest time point that data was available. For outcomes where 52 weeks was the longest time point that data was available, this data was extracted. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. We appreciate that with the large amount of evidence, it becomes very difficult to pinpoint which studies contribute to each finding. An asterisk has been added under each GRADE table footnotes to clarify which studies contribute to each

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					comparison. Where data from more than one study has been pooled together in meta-analysis, this is displayed in the second column of the GRADE tables (number of studies) together with the total number of participants from the combined studies and the follow-up timepoint at which the outcome was assessed. Apart from the GRADE tables, which studies contribute to each different comparison and outcome are also displayed in the forest plots available in Evidence review H: Appendix E.
The Royal College of Psychiatrists	Evidence review G	324	030	*No clinically important difference was seen for return to school (measured in hours attended) and adverse events* We draw attention to the way that the evidence synthesis is obscuring the meaning of the adverse events data. On first reading it seems to be saying "Not clinically important". To include in the same sentence the claim that there was no difference in school attendance, which if correct could indeed be evidence of the ineffectiveness of CBT, seems to suggest a second ineffectiveness – that it was ineffective in producing adverse events. Which of course is nonsense. This is something that happens repeatedly in the evidence synthesis sections for both CBT and GET – the true meaning of what is an important positive findings of the trials, is obscured by the syntax of the sentences so that both the committee and indeed any reader would easily miss the significance of what is being reported. Does NICE agree this is a misleading way of presenting important data and should be changed?	Thank you for highlighting this. The wording in the report has been amended.
The Royal College of Psychiatrists	Evidence Review G	325		The committee have recommended that CBT should not be used to treat ME/CFS, but only to treat emotional distress arising as a consequence of illness. They particularly seem to object to the idea that CBT might be used to treat core symptoms of ME/CFS such as fatigue. But CBT is used successfully to treat fatigue in stroke and multiple sclerosis as a recent meta analyses confirm (pubmed.ncbi.nlm.nih.gov/32106490 and multiple sclerosis (https://pubmed.ncbi.nlm.nih.gov/31780252/).	Thank you for your comment. After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case.

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				It is not assumed that stroke or MS are psychological conditions or that CBT should only be used to treat distress and not fatigue given that CBT does reduce fatigue. The main reasons put forward by the panel is that some people either feel themselves or are told by others that be offered GET or CBT is tantamount to saying that you were not really ill, that this was all in the mind and so on This misperception is not a reason to remove a treatment. NICE is now in a good position to help dispel this myth. It is reasonable to draw attention to the distress such misunderstandings have caused, but the opportunity to resolved such misunderstandings as not been taken. Will NICE please now take the opportunity to correct these misunderstandings about CBT?	CBT is a supportive psychological therapy which aims to improve wellbeing and quality of life. The evidence reviewed within the present guideline did not show that CBT can have a clinical benefit in terms of fatigue, and the current evidence base is not sufficient to draw conclusions about the effect of CBT on fatigue experienced in ME/CFS. However, the committee acknowledge the usefulness of CBT in the management of symptoms of ME/CFS which can also include fatigue and this is conveyed in the recommendations.
The Royal College of Psychiatrists	Evidence Review G	325	039 onwards	NICE will also have to consider what impact this might have had on the consultation around CBT and the decision not to make it available as a treatment. The key evidence to support or refute this – whether or not CBT has an influence on a primary endpoint and/or critical outcome is central to answering that question. If in addition it is agreed that the wrong outcome was calculated for CBT versus usual care in at least two studies, and wrong ratings made of precision, we think this is not a small error, but a substantial one, affecting one of the two key decisions taken by the Review, rejecting GET and weakening CBT.	Thank you for your comment. After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case.
The Royal College of Psychiatrists	Evidence Review G	328	038	*the committee noted that none of the evidence included or reflected the needs of people with severe or very severe ME/CFS. They recognised that CBT could be supportive for people with severe or very severe ME/CFS but because of the severity of their symptoms it is important to be more flexible and adapt the delivery of CBT to accommodate the limitations of those with severe or very severe ME/CFS. This might include shorter, more infrequent sessions and longer-term goals.*	Thank you for your comment and information

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				Whilst there are in fact there are case reports and series of those with very severe ME/CFS (wheel chair or housebound) who have improved after CBT we agree with this observation.	
The Royal College of Psychiatrists	Evidence review G	332 333	021 - 045 001 - 009	The Cochrane review of exercise therapies provides a different interpretation of benefits than this review, one of the main reasons being because it considered outcomes at the end of treatment across all trials, which this review failed to do (Larun et al, 2019, DOI: 10.1002/14651858.CD003200.pub8). This review summary interpretation by the committee would be substantially different if end of treatment outcomes were properly and consistently reviewed and considered for all trials of GET (see more detailed comments on review H below) Could these be corrected please?	Thank you for your comment. Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. Data was extracted at the longest follow-up available, as specified in the protocol for this review. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

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					To note this Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review.
The Royal College of Psychiatrists	Evidence review G	333	011 - 050	It is a remarkable contrast that the quality of these qualitative studies were regarded as moderate or low, whereas RCTs of GET were regarded as low or very low. This is in spite of the many varied ways in which patients were recruited to these qualitative studies, with a range of establishing diagnoses, few made with the same stringencies applied by RCTs. A lot of findings have been cited from Cheshire and colleagues (2018, https://doi.org/10.1080/09638288.2018.1499822), but this was from the one trial of guided self-management, based on GET, not therapy delivered GET, as tested in the other nine or so trials. So comments made may not apply to GET delivered as a therapy. "Individuals who have been ill with ME/CFS for a relatively longer period of time and/or have additional comorbid conditions may benefit from more bespoke therapies with greater health professionals input, delivered by appropriate therapists." (Cheshire et al, 2018, cited above). Could this be clarified please?	All NICE guidelines follow the process for quality assessment of the evidence as set out in Developing NICE guidelines: the manual. Qualitative evidence is assesses using the GRADE CERQual approach This guideline was no exception. Limitations across quantitative and qualitative studies can vary, resulting in different levels of evidence quality or confidence in the evidence. Please note that evidence quality is only one of the many factors that the committee take into account in decision making. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of

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					evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. This resulted in further downgrading many qualitative studies for additional concerns over the applicability of the included population which in turn resulted in concerns over relevance of the findings

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					emerging from those studies and lowering the overall assessment of confidence in many qualitative findings (this has been reflected throughout the report for Evidence review G, with details of the PEM re-analysis and changes to the quality of the evidence included across the relevant evidence sections). The Cheshire study in particular, was not downgraded for concerns over applicability as it included participants from the GETSET trial meeting the NICE criteria that include PEM as a compulsory feature but part of the qualitative evidence for GET and other exercise interventions was downgraded from moderate to low confidence and from very low to low confidence. We have stratified the qualitative evidence by intervention type in line with what had been pre-specified in the review protocol (see Appendix A- Review protocols, Evidence review H). Despite findings from different exercise interventions summarised together, the committee discussed GET in detail separately as it has been reflected in the Committee's discussion and interpretation of the evidence section in Evidence review G. Also in line with NICE methods (see Developing NICE guidelines: The manual) Findings from the quantitative evidence have been summarised on a comparison basis meaning that only studies looking at similar interventions and comparisons have been summarised together. Apart from the findings emerging from both the qualitative and the quantitative evidence, the committee utilised their clinical experience to inform decision making that has been based on the consideration of multiple factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact, clinical and patient experience and equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The committee recognise that

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					each individual may differently benefit from interventions and this has been acknowledged in the recommendations that have included specific recommendation about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. The same has been applied to CBT.
The Royal College of Psychiatrists	Evidence review G	334	045 - 049	*"The committee discussed potential reasons for this and noted the limitations of the clinical evidence including, the low to very low quality, the heterogeneity in the GET interventions, the lack of clarity over the intervention components, potentially different recruited populations and outcomes being measured differently across the studies and the difficulty in combining any of the studies. This picture was also reflected in the evidence that compared GET to other interventions. The committee's discussion and interpretation of the evidence compared GET to other interventions. The committee agreed that the same limitations applied and in addition the heterogeneity in the other comparisons made it difficult to make confident conclusions about the evidence."* If the review of the trials of GET had not omitted important outcomes, such as those at the end of treatment and trial follow up (absent in White, 2011), then these limitations would have been fewer, with far less imprecision for fatigue, physical function, overall disability and overall health. If the review of trials of GET had not down-graded all but one trial of GET on the questionable basis of indirectness (down-grading trials that did not mandate PEM), then all these trials would have been promoted by one level in quality. Regarding "potentially different recruited populations", all GET trials used either CDC criteria or Oxford criteria, mostly recruited	Thank you for your comment. <u>Cochrane review, meta-analysis and outcome timepoints</u> Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. Data was extracted at the longest follow-up available, as specified in the protocol for this review. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more

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				from secondary care. Recruiting from different populations and showing the same results could be regarded as a strength rather than weakness. Regarding outcomes and problems combining them, the Cochrane review had no difficulty undertaking a meta-analysis of these trials (Larun et al, 2019, cited above), Regarding comparisons of GET against other interventions, the Cochrane review show these results in some detail (Larun et al, 2019, cited above). In the light of these observations, would NICE care to review their conclusions here?	helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. . This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. *PEM and indirectness* The committee agreed that PEM was a key feature of ME/CFS and that people with PEM may react differently to interventions compared to people without PEM. They considered that previous criteria, such as the Oxford Criteria and 1994 CDC criteria identify a heterogeneous population, which may or may not include people with ME/CFS (See Evidence review D – diagnosis). The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential

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					feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Evidence review G	334	045 - 049	NICE were also sent before the deadline for accepting new evidence the latest individual patient data meta-analysis. The IPD replicates and extends the findings of the aggregate review (Larun 2019) that GET improves both fatigue and physical function by end of treatment. How does the results of the IPD affect NICE's conclusions?	Thank you for your comment. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. It is not an IPD.
The Royal College of Psychiatrists	Evidence review G	334	042 - 045	"*The committee noted there was no clear picture of benefit, and the evidence was inconsistent with outcomes that showed benefit in one study showing no clinically importance difference in other studies.*" The Cochrane review of exercise therapies found clear and consistent evidence of benefit by the end of treatment on primary outcomes of fatigue and physical function (Larun et al, 2019, DOI: 10.1002/14651858.CD003200.pub8). In view of the errors made in this review (not showing end of treatment outcomes in	Thank you for your comment. *Time points* Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline

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				all trials, and reducing generalisability of results by down-grading non-PEM criteria trials), an impartial judge might be more likely to prefer the Cochrane interpretation. Would NICE agree that the review shows a partial view of the evidence for the benefits of GET?	was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline . *Cochrane* This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as

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					usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Also note that Cochrane has acknowledged issues with this review in terms of the methods used and the population definition and they plan to conduct a full update of this Cochrane review. *<u>PEM and indirectness</u>* The committee agreed that PEM was a key feature of ME/CFS and that people with PEM may react differently to interventions compared to people without PEM. They considered that previous criteria, such as the Oxford Criteria and 1994 CDC criteria identify a heterogeneous population, which may or may not include people with ME/CFS (See Evidence review D – diagnosis). The committee do not assume that people recruited to trials do not experience PEM they just don't know if the information is not reported, and numbers of people with PEM are rarely reported in the trials. This causes difficulty in interpreting the evidence from trials that do not use a criteria that has PEM as an essential feature (and therefore a 100% ME/CFS population) or where the percentage of people with PEM are not reported. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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The Royal College of Psychiatrists	Evidence review G	334	001 - 003	"*Some found the information booklet helpful, whereas others found it patronising, having the feel of marketing material or seemingly designed for participants with a higher level of functioning.*" The negative observations were reported by 2/19 participants of Cheshire et al, 2018, cited above. The summary review of this study also needs to make explicit that it stratified sampling to include both those who improved and those who did not. Could this be clarified please?	Thank you for your comment. It has been specified in relevant sections of the qualitative evidence tables (Appendix D, Evidence review H) and in the table of included studies (Evidence review G) that the study included both people who improved and people who deteriorated. When reviewing qualitative evidence, we carefully consider the information reported in each paper and extract all the information relevant to the review topic, regardless of whether it reflects positive or negative experiences of the interventions received and synthesise them into different review findings to capture the multiplicity of experiences people may have. Positive accounts emerging from the Cheshire study have been synthesised and contribute to different review findings that the committee has considered, Negative experiences including the statements you refer to also emerged from the study. These are equally considered by the committee regardless of how many people reported this as they also reflected the experience of some people. Please note that this was only part of the information that the committee has considered. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
The Royal College of Psychiatrists	Evidence review G	334	038 - 040	"*The committee noted the outcomes showing benefit were mainly measured at a relatively short follow up period of around 12 weeks.*" This is because this review completely omitted to provide primary outcomes and important secondary outcomes of the largest trial	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set

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				of GET (White et al, 2011, cited above), which provided outcome data at end of treatment (24 weeks) and follow up while still in randomised groups (52 weeks). Addition of these data would considerably improve imprecision and thus up-grade these results, and the confidence in them. We cannot comprehend why the committee did not then continue. "However such data was available to us and showed……" Failure to do that is both unfair and misleading Would NICE agree that a more complete and transparent review of this evidence would change GRADE ratings?	out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. . Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. . For outcomes where long-term follow-up was available (134 weeks), this data was preferentially extracted in line with the review protocol, as this was the longest time point that data was available. For the remaining outcomes, 52 weeks was the longest time point that data was available, and this data was extracted. Available 24-week outcome data was not extracted, as this time-point was not the longest time-point available. Please note that imprecision is only one element of quality assessment which has also been downgraded for risk of bias and serious population indirectness after further scrutinising the information on PEM available about study populations, following the consideration of stakeholder comments. Consideration of outcome data at 24 weeks would therefore not result in higher quality evidence or changed the GRADE ratings. Also, evidence quality is one of the many factors the committee considers in decision making, along with factors including the types of

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					evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). As a result, the inclusions of data from an earlier time point would not change the recommendations made.
The Royal College of Psychiatrists	Evidence review G	334	037 - 038	*"The committee noted that overall, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects."* This is because trials of GET were illogically down-graded on the basis of indirectness, which goes against the PICO population instruction (see above), and reduces the generalisability of these guidelines, which no longer cover all patients diagnosed with ME/CFS. It is also wrongly applied. Could this be corrected please?	Thank you for your comment. The committee agreed that PEM is a defining feature of ME/CFS and the response to an intervention is likely to be different in people who have PEM compared to those who do not. Lack of PEM raises concerns about the extent to which the population included in a study represents people who actually had ME/CFS. It is the presence/absence of PEM that impacts the applicability and generalisability of the evidence identified to populations with ME/CFS rather than the act of downgrading the evidence due to the identified concerns. Acknowledging those concerns through downgrading the quality of the evidence strengthens the quality standard of the guideline ensuring that factors influencing the extent to which the evidence accurately reflects the experience of the population of interest are adequately considered. Please note that indirectness is only one element of evidence quality which is also determined by risk of bias, inconsistency and imprecision and the effectiveness evidence for GET has also been downgraded due to risk of bias with many outcomes also downgraded for imprecision in the effect estimates. Also, evidence quality is one of the many factors that the committee take into account in decision making, along with factors including the types of evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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					In response to stakeholder comments criticising the methods used for downgrading studies for population indirectness based on the diagnostic criteria used and whether or not this criteria had PEM as a compulsory feature, we looked for any published information on the percentage of participants with PEM in the included studies, and undertook a reanalysis. As part of this the committee agreed that any evidence with a population ≥_95% with PEM_would be considered direct but the quality of evidence not meeting this requirement would be downgraded. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee considered that the overall results of a study were unlikely to be significantly affected by participants without PEM when the above threshold was met.
The Royal College of Psychiatrists	Evidence review G	334	040 - 041	*"The benefits may have been a result of initial improvements in energy management and then potentially not been sustained*." This sentence is pure speculation and not based on any evidence. The PACE trial showed a significantly greater increase in metres walked in the six minute walking test, 12 months after randomisation, in those who had received GET compared to both specialist medical care and adaptive pacing therapy (APT) (White et al, 2011, cited above). Those who received APT walked a mean of 20 metres more by this time, compared to a mean of 67 metres more by those who had had GET. We suggest the statement is deleted,	Thank you for your comment. This is the summary of the committee's interpretation of the evidence and has not been deleted.
The Royal College of Psychiatrists	Evidence review G	334	041 - 042	"*This was supported by outcomes measured at longer term follow up points not demonstrating the same benefits."* This is not the case. The two trials of long-term follow up of GET have shown maintenance of the benefits of GET beyond the end of trial follow up, in naturalistic follow up studies.	Thank you for your comment. *Follow up data* Study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial

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				Powell et al (2004, https://doi.org/10.1192/bjp.184.2.142) found no significant difference in the proportions meeting trial criteria for CFS at long-term (2 years) compared to short-term follow up, after variously delivered exercise therapies in an RCT, and concluded that: "Benefits of the intervention were maintained at 2 years." Sharpe et al (2015, https://doi.org/10.1016/S2215-0366(15)00317-X) found no significant differences in the primary outcomes of fatigue and physical function between long-term (2.5 years) and short-term follow up (1 year) for GET. Their interpretation was: "Improvements in fatigue and physical functioning reported by participants originally assigned to CBT and GET were maintained." It is true that there were no significant differences in primary outcomes at 2.5 year follow up between GET and both SMC and APT, in the PACE trial, but that comparison was made 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did, as the data confirms). "210 (44%) participants received additional treatment (mostly CBT or GET) after the trial; with participants originally assigned to SMC alone (73 [63%] of 115) or APT (60 [50%] of 119) more likely to seek treatment than those originally assigned to GET (41 [32%] of 127) or CBT (36 [31%] of 118; p<0·0001)" (Sharpe M et al, 2015. http://dx.doi.org/10.1016/S2215-0366(15)00317-X). The participants who had received APT and SMC had "caught up" with those who had received GET, but, since randomisation had been abandoned 18 months previously no one can explain why that might have been, and patient choices made at the end of the trial follow up, 18 months earlier, may have helped to explain this. Could this be corrected please?	authors subsequently published long-term follow-up data at 134 weeks for some outcomes. The long term follow up data from the PACE trial has been included. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. Powel et al 2004 . The data has not been extracted because there was no appropriate comparator (participants from the control group had received the intervention) so it didn't meet protocol. Sharpe 2015 et al 2015. Additional therapy had been given according to physician choice and patient preference after 1-year so it is unclear to which intervention findings can be attributed to.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

Consultation on draft guideline - Stakeholder comments table

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The Royal College of Psychiatrists	Evidence review G	334	031	*"In terms of effectiveness, evidence was conflicting,…"* One cannot use qualitative studies to make any observations about effectiveness. We are surprised that it has not already been challenged Could this be corrected please?	**Thank you for highlighting this. The wording of this sections has been amended.**
The Royal College of Psychiatrists	Evidence review G	335	030 - 044	This approach is not supported by any significant trial evidence, in fact there is evidence against it. It is based on a non-physiological understanding of physical and mental energy. The College believes that NICE should reconsider this guidance on the basis of the lack of evidence to support it. There is a remarkable contrast in this draft guidance, which was absent from the 2007 NICE guidelines, to reject interventions for which there is reasonable evidence, and yet accept and recommend interventions for which there is little supportive trial evidence. The College recommends that NICE should reconsider this recommendation as a consequence.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result

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					in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
The Royal College of Psychiatrists	Evidence review G	335	010 - 016	*"The committee agreed that the term 'GET' should be avoided as it has significant negative connotations amongst people with ME/CFS, largely due to GET programmes that have fixed continued increases in activity despite patients reporting a worsening of their symptoms. The committee made this clear and made a recommendation that any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy should not be offered to people with ME/CFS."*	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality

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				Firstly, where is the evidence from patients who actively seek out GET, and are satisfied to receive it? In the PACE trial, 88% of participants were satisfied with receiving GET (White et al, 2011, cited above). See also: Action for ME (2011a) You say 'Save our services!' (Survey results). InterAction 77: 4–5. https://www.actionforme.org.uk/uploads/pdfs/you-say-save-our-services.pdf. In this survey of a patient support group members, 48% of 775 patients surveyed wanted GET to be available on the NHS, compared to 32% who did not. Secondly, and most importantly, where is the evidence of *"GET programmes that have fixed continued increases in activity despite patients reporting a worsening of their symptoms"*? GET programmes in trials do not do this (see comment above). The College is aware of patent support group surveys suggesting that this can occur, but Gladwell and colleagues (2013, DOI: 10.3109/09638288.2013.797508) showed that this was related to exercise programmes that were not consistent with the NICE guideline description of GET (NICE, 2007). Any medical treatment can cause harm if given at the wrong dose or frequency, but we do not ban such treatments as a consequence. The College agrees that GET programmes should not necessitate "fixed continued increases in activity", but it does not follow that means banning GET, since published GET programmes, including that recommended by NICE in 2007, do not include such advice.. We would welcome any recommendations from NICE about how to improve or monitor standards, to prevent poor practice in exercise therapy, and hope that the Committee will recommend a national programme of quality improvement, such as that promised in 2007, but which we understand proved short lived.	and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The

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					committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
The Royal College of Psychiatrists	Evidence review G	335	016 - 020	"*Many members of the committee felt that the term 'exercise' should also be avoided as this could easily be misinterpreted by patients and practitioners and could lead to people undertaking non-ME/CFS-specific exercise programmes that could be harmful to them. The distinction between exercise and physical activity was highlighted in the terms used in the guideline.*" The College is not averse to considering describing GET as a physical activity programme, since good GET incorporates exercise into everyday activities of living. Since exercise is simply activity that requires exertion, GET programmes most commonly involve walking, which can be incorporated into ADLs, such as housework or walking to the shops. At the same time, it is important to remember that the trial evidence is about GET, and should be described as such. Furthermore, some patients will want to incorporate exercise into their later programmes, such as jogging, cycling and swimming, which are more accurately described as exercise than physical activity. What is most important is to explicitly and carefully describe this treatment in the way that NICE did so in 2007. The College agrees with lines 23 and 24 about *"the requirement to provide clarity and clear guidance around activity."*	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and

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					exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits:

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					- on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. - the section on physical activity now includes exercise - Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed).
The Royal College of Psychiatrists	Evidence review G	335	025 - 029	*"The committee agreed that energy management is one of key tools that people with ME/CFS have to support them in managing and living with the symptoms of ME/CFS. Energy management is not a physical activity or exercise programme although the principles of energy management apply to physical activity programmes."* There is insufficient evidence to support "energy management" (a.k.a. pacing) as a key tool. As mentioned above, and the evidence review confirms, what trial evidence there is finds such an approach either lacking benefit or harmful. The College recommends that NICE should reconsider this recommendation as a consequence.	Thank you for your comment. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. The committee took great care to ensure that there was consistency in decision making across the level and amount of evidence underpinning recommendations. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual,

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					section 9.1 for further details on how recommendations are developed). Although the quantitative evidence identified on self-management was limited and no evidence was identified on people's experiences of self-management interventions in the qualitative review of experiences of interventions, from evidence identified for other interventions that encouraged self-management techniques, people appeared to value and benefit from this type of support. After considering the evidence identified for self-management, as well as the lack of information and support people with ME/CFS report in managing their symptoms emerging from Evidence review A the multiple factors mentioned above and their clinical experience, the committee agreed the evidence was unclear but recognised the benefits of self-management strategies for people with ME/CFS and the importance of having access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (see Evidence review G for the committee discussion on self-management strategies). Based on their experience, the committee agreed that energy management is one of the most important tools that people with ME/CFS have to support them in living with the symptoms of ME/CFS. Withing this framework, they made recommendations including strategies of energy management to provide people with such support. The committee recognise people may benefit from different self-management strategies and that these should be discussed and agreed with the person with ME/CFS to support them in developing a care and support plan that is tailored to their individual needs as reflected in the recommendations.

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The Royal College of Psychiatrists	Evidence review G	335	045 - 048	"*The committee raised concerns regarding the theory of deconditioning that underpins GET, which they considered cannot be applied to people with ME/CFS. This is raised throughout the guideline and the principles of care for people with ME/CFS state that people with ME/CFS should be believed and they should be reassured their condition is real.*" No one claims that deconditioning causes ME/CFS – if anything there is some evidence that over training is more of an issue. It should be stressed that the College could not find any studies that would suggest that deconditioning is a cause of ME/CFS. So we fail to why consideration of any deconditioning present in patients with ME/CFS should call into question patients being believed regarding their illness and its reality. The issue that needs to be discussed is whether it is possible that ME/CFS leads to deconditioning, in other words a secondary handicap well recognised in rehabilitation. There is systematic review evidence that patients with ME/CFS are less physically active than healthy controls (Evering et al, 2011, https://doi.org/10.1177%2F0269215510380831), and some probably do suffer from deconditioning (Nijs et al, 2011, https://doi.org/10.3109/09638288.2010.541543; Franklin et al, Int J Sports Med 2019; 40(02): 77-87, DOI: 10.1055/a-0802-9175). This is hardly a surprise since sedentary behaviour will tend to lead to deconditioning and its health consequences (WHO, 2020, cited above). It is true that some GET programmes have in the past either been designed to help reverse deconditioning or deconditioning has been cited as a reason for starting GET. However, the largest mediation study of GET showed that a change in fitness does not mediate effective GET (Chalder et al, 2015, http://dx.doi.org/10.1016/S2215-0366(14)00069-8). Whereas GET was strongly mediated by improved exercise	Thank you for your comment. Thank you for your comment that ME/CFS is not caused by deconditioning. The Committee agree with this. However, the committee noted that in some cases 'GET was implemented on the basis of deconditioning and exercise avoidance theories of ME/CFS. These theories assume that the syndrome is perpetuated by reversible physiological changes of deconditioning and avoidance of activity'. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility.

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				tolerance (Chalder, 2015). So addressing deconditioning does not seem to be important in GET in order for it to help. Could these statements therefore be revised?	
The Royal College of Psychiatrists	Evidence review G	335	003 - 005	"*The committee noted that no harms were identified in the clinical evidence but also noted these were rarely included as an outcome and reported.*" Two trials reported by the review provided systematic assessments of six safety outcomes (non-serious adverse events, serious adverse events, serious adverse reactions to treatment, deterioration in global health, deterioration in physical function, withdrawal from treatment), finding no excess harms associated with GET, in comparison with control interventions (White et al, 2011, https://doi.org/10.1016/S0140-6736(11)60096-2; Clark et al, 2017, https://doi.org/10.1016/S0140-6736(16)32589-2). There was one exception - SAEs were more common in GET participants in one trial in comparison to specialist medical care participants, but independent scrutineers did not attribute these SAEs to GET (White et al, 2011). There was no significant difference in numbers reporting SAEs after GET compared to adaptive pacing therapy (White et al, 2011). These two trials recruited 852 patients, 267 of whom received GET or guided self-help based on GET. The safety data for both of these trials applied the standard protocols required by the European Union Clinical Trials Directive for medicinal products (https://ec.europa.eu/health/human-use/clinical-trials/directive_en). It is hard to think of more stringent methods to measure safety. If NICE are still concerned about safety and regard these results as insufficient to be confident about the safety of GET, most published GET trials contain further outcomes that would inform this issue. These outcomes include numbers withdrawing from	Thank you for your comment. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable.. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.

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				treatment, numbers dropping out of trial follow up, and numbers rating their overall health as "much" or "very much" worse. Would NICE care to review these data?	
The Royal College of Psychiatrists	Evidence review G	335	005 - 007	"*The committee reflected that in contrast harms such as worsening of symptoms were reported in the qualitative evidence and took this into consideration when making recommendations on physical activity and exercise.*" Similar to not being able to assess efficacy from qualitative studies, it is unwise to assess harms from qualitative studies, when the more reliable alternative of trial data is already available. Qualitative studies are rarely if ever the last word in deciding the overall balance of harm and benefit, they provide a signal for quantitative data to confirm or refute. The committee should revisit Cheshire et al 2018, which they quote liberally in the qualitative review, purposively sampled all ten of 107 participants who had received guided self-help based on GET principles, who had also deteriorated (albeit only "a little worse" since no one in this GETSET trial had rated themselves as "much" or "very much" worse). This means that there was a purposive selection bias in this qualitative study, which the committee need to consider before relying on these qualitative data to make recommendations about the harm of GET. Could this be corrected please?	Thank you for your comment. The use of qualitative evidence in this guideline has been no different to other NICE guidelines where there is limited quantitative evidence. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations, using a range of evidence . When developing this guideline the committee considered a wide range of evidence apart from qualitative evidence, including that from, published peer review, quantitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee used its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The balance of perspectives and experiences on the committee ensures that reflexive practice is inherent in its decision making. The committee considered many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Considering all the evidence available, people's perceptions of harm and negative experiences emerging from the qualitative experiences of interventions review have been taken into account in decision making. The text you refer to in Review G has been edited to clarify it is people's perceptions of harm that are reflected in the qualitative evidence. The Cheshire study included a mixed group of participants who had rated themselves as improved and participants who had rated themselves as

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					deteriorated after the intervention and has therefore not been downgraded for concerns over selection bias.
The Royal College of Psychiatrists	Evidence review G	335	008 - 010	*"Concerns were raised regarding the definition of GET, as there is no standard definition and there have been a range of different interpretations. This was reflected by the heterogeneity in the interventions described in the studies."* GET as delivered in all the trials of GET was well described and adhered to since the first RCT of GET back in 1997. Fulcher and White (1998, https://doi.org/10.1016/S0031-9406(05)65554-X) first published a guide on how to provide GET in 1998. Most trials have incorporated these principles, such as starting at low intensity, incremental increases in duration of exercise, depending on symptoms, before increasing intensity later, and using heart rate monitors to monitor the safe intensity of exercise. The PACE trial website provides links to freely available and detailed therapist and patient manuals describing GET, which was found to be safe in this trial (https://www.qmul.ac.uk/wolfson/research-projects/current-projects/projects/pace-trial.html). Could this be corrected please?	Thank you for your comment. The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
The Royal College of Psychiatrists	Evidence review G	336 337	043 - 050 001 - 007	The College agreed that physical activity programmes should only be provided for patients who wanted them, and that specialist therapists, such as physiotherapists, are the best HCPs to support and provide them.	Thank you for your comment.
The Royal College of Psychiatrists	Evidence review G	336	036 - 042	The College also agrees that wearable devices that measure activity and other physiological variables can be a useful adjunct to rehabilitation for patients with ME/CFS.	Thank you for your comment.
The Royal College of Psychiatrists	Evidence review G	336	027 - 032	"*The committee commented on the findings in the qualitative evidence that people had felt pressured and blamed when they could not complete the programme even though it was making*	Thank you for your comment.

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				their symptoms worse. The committee acknowledged the controversy around the setting of fixed unrealistic goals and the importance of understanding realistic goal setting by both the person with ME/CFS and the healthcare professional supporting any programme." The College strongly agree with NICE that no patient should every feel pressured or blamed for not completing a therapy. It also agreed that unrealistic goal setting is unhelpful.	
The Royal College of Psychiatrists	Evidence review G	337 338	034 - 051 001 - 002	*An ideal physical activity programme:* While the College supports NICE's ambition to describe an ideal physical activity programme, we question whether the evidence supports what is currently recommended. The College suggests that such a programme should be based on the principles of GET, as described in the PACE and GETSET trials, which have been shown GET, and self-management based on GET, to be moderately effective and safe.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). After reviewing the evidence available, together with their clinical experience, and considering the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. The committee recognise that each individual may differently benefit from interventions and this has been acknowledged in the recommendations that have included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing more specific recommendations on the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that

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					had been identified in the qualitative evidence and their own experiences of these types of interventions.
The Royal College of Psychiatrists	Evidence review G	337	025 - 033	While the College agrees with almost all of this sensible advice about not undertaking an unsupervised exercise programme, etc, it suggests that NICE remove its statement that includes GET in this paragraph, since what it attributes to GET is not valid, as noted above.	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects

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					the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
The Royal College of Psychiatrists	Evidence review G	337	008 - 009	"*The committee discussed that people with ME/CFS react significantly differently to physical activity compared to healthy people and people with other medical conditions*." While the College agreed that people with ME/CFS react to physical activity differently to healthy people, we question whether there is sufficient evidence that that reaction is different from people with other medical conditions, particularly since PEM is reported by patients with other medical conditions, such as fibromyalgia and mild traumatic brain injury. We suggest that NICE reconsider this statement, which divorces this illness from the rest of medicine. But we do agree that programmes designed solely for healthy people to get fitter, which are self-directed and unsupervised, should not be recommended for those recovering from ME/CFS.	Thank you for your comment. This paragraph reflects the discussion the committee had and has not been edited. To note the committee emphasise it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).
The Royal College of Psychiatrists	Evidence review G	338	003 - 022	Physical maintenance: "*They noted it is important that where appropriate people with ME/CFS have management plans for physical maintenance, symptom control or restoration of physical ability.*" The College agrees with NICE regarding the vital importance of such a programme. It is called graded exercise therapy, which has been shown to restore physical ability".	Thank you for your comment.
The Royal College of Psychiatrists	Evidence review G	338	026 - 039	The College agreed with NICE about the importance of supporting patients severely affected by ME/CFS. We agree that their progress will be slow and that specialist therapists, such as	Thank you for your comment.

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				physiotherapists and occupational therapists can play an important role in helping them improve their mobility and function. Where we disagree is in the means to achieve this, as mentioned above.	
The Royal College of Psychiatrists	Evidence Review G	342	032	"*After discussing the clinical effectiveness of non-pharmacological interventions and people's experiences and considering the reports from the young people and people with severe ME/CFS the committee agreed there is no current non-pharmacological treatment or cure for ME/CFS"* The College disagree with this. The evidence that CBT is a treatment for ME/CFS, which will be covered more by the RCPCH and our Child and Adolescent Psychiatry colleagues, seems to us to be compelling. Would NICE please comment?	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
The Royal College of Psychiatrists	Evidence Review G	342	036	"*The committee discussed the claims that have been made about cures for people with ME/CFS and lack of conclusive evidence for this. The committee were aware of interventions that are promoted as cures and there is often a financial cost when these are pursued. To address this the committee made a recommendation to raise awareness that there is no current non-pharmacological treatment of cure for people with ME/CFS*" The meaning of this passage is unclear to us. It seems that the committee is taking a view on whether or not people should pay for therapy. The costs of interventions are not considered by NICE in their deliberations unless they exceed the standard QALY measures. We do not think that NICE should be *'making people aware that there is no non-pharmacological treatment or cure '* because first we believe that GET and CBT are treatments, when done	Thank you for your comment. The committee is referring to interventions claiming to cure ME/CFS that people with ME/CFS pursue outside of the NHS. Some of these do have a financial cost for the individual. This is clear in the rationale for the recommendation and the text in the evidence review has been edited to clarify this. *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this.

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				properly. Second, the rich illness perception literature tells us that this would have a deleterious effect not just on patients' well-being in general, but probably also on outcomes of the illness itself. Ignoring a large literature in health psychology does not negate it. This statement therefore should be reconsidered	Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
The Royal College of Psychiatrists	Evidence review G	342	039	One of the recommendations of the committee is that NICE should raise awareness that there are no non-pharmacological treatments for ME/CFS. If NICE is in the business of raising awareness, then instead of trying to reduce or indeed stop all together the uptake of and access to non-pharmacological treatments for CFS, it might be better employed raising awareness of the misunderstandings that still exist around non-pharmacological treatments for ME/CFS instead? Would NICE please comment?	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
The Royal College of Psychiatrists	Evidence Review G	342	041	*In addition, the committee made 'do not' offer recommendations for CBT, therapy based on physical activity or exercise therapies derived from osteopathy, life-coaching and neuro-linguistic programming (for example the Lightning Process), and supplements to treat or cure ME/CFS.* We do not understand why CBT is included here, since the committee is making a recommendation in favour of it, albeit with limitations with which we strongly disagree. The recommendation not to offer therapy based on physical activity demonstrates once again some of the confusions in this document. This recommendation required reconsideration.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However, while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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The Royal College of Psychiatrists	Evidence review G Evidence Review H	321	3.3 Table 4	There is an error in the Deale et al trial data. The trial showed at its primary six month end point significant benefit for fatigue (rated in two ways), global improvement rating of being better or much better, psychological status, depression, physical functioning, general symptom and return to work; there was also a low risk of imprecision. However, in the summary (Evidence Review G p324, line 2), this was reported as being no difference in physical functioning and fatigue. The Deale et al trial is also misrepresented in that it reads as if it was a head to head comparison with relaxation therapy. But relaxation therapy was chosen as an active placebo intervention to control for therapist time, a major confounder of psychological intervention trials. The committee should have been aware of the role of relaxation therapy in this context and interpreted the results in that light, but did not. It and other trials with similar designs (basically comparing with active placebos, as in some of the Dutch trials) should have been pooled so that a fairer impression of the effect of CBT could have gained. Could this be corrected?	Thank you for your comment. The wording in this section has now been amended for clarity. Clinical benefit was found for global improvement of change rating, fatigue (chalder fatigue scale and fatigue problem rating), physical functioning (SF general health survey physical functioning) and return to school or work (work and social adjustment scale and part time or full time employment). There was no clinically important difference for psychological status (Beck depression inventory and general health questionnaire). Note that clinical benefit or harms for each outcome are determined based on the minimally important difference (MID), not statistical significance or benefit/harms reported by study authors. Imprecision is considered separately to clinical importance but is also assessed using the MIDs. It is a measure of the width of the confidence interval for an effect estimate in relation to the MID, not statistical significance. Imprecision is often a reflection of studies with small sample sizes or low number of events, which results in wide confidence intervals around effect estimates resulting in uncertainty around the results. Detailed information on this process can be found in the methods chapter, and the MIDs used are in Appendix K of Evidence review H. Regardless of whether the relaxation therapy was considered an 'active placebo' by study investigators, it is still an intervention that the participants received. The committee understand that active control arms are sometimes used in trials of psychological therapies to control for the effect of therapist time/interaction, but this does not make active control arms equivalent to control arms such as waiting list, or usual care, as there may still be an effect of the treatment. It would be misleading to pool such studies.

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The Royal College of Psychiatrists	Evidence review H	290 - 291	Figure 119- 121	Finding no significant differences in either non-serious adverse events, serious adverse events, or serious adverse reactions to treatment in the largest trial to compare CBT and GET suggests that GET has no more evidence of harm than CBT. So where is the trial evidence that justifies banning it? We request a reconsideration of this judgement please.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).After reviewing the evidence available, together with their clinical experience, and considering the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. The committee recognise that each individual may differently benefit from interventions and this has been acknowledged in the recommendations that have included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing more specific recommendations on the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.
The Royal College of Psychiatrists	Evidence review H	316 - 317	Figure 241 - 243	Finding no significant differences in non-serious adverse events, serious adverse events, and serious adverse reactions to treatment in two large trials suggest that GET has no more evidence of harm than specialist medical care. So where is the trial evidence that justifies banning it? We request a reconsideration of this judgement please.	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and

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					harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).After reviewing the evidence available, together with their clinical experience, and considering the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. The committee recognise that each individual may differently benefit from interventions and this has been acknowledged in the recommendations that have included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing more specific recommendations on the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.
The Royal College of Psychiatrists	Evidence Review H	031	Appendix D - Effectiveness evidence	The studies of Knoop et al, 2008; Neijhof et al, 2012 and Janse et al, 2018 (reference 409, 536 and 352 respectively are not described in the appendix. This makes it impossible to determine how these studies were evaluated. Can NICE please correct?	Thank you for pointing this out, and apologies for any confusing this might have caused. These were missing in error and have now been added back into the review (see appendix D of evidence review H).
The Royal College of Psychiatrists	Evidence Review H	209	Appendix D – Effectiveness evidence	Stulemeijer et al., 2005: "Seriousness indirectness of study". PEM is not a compulsory feature. However, 68/71 (96%) of participants reported PEM. A subgroup analysis of the patients who reported PEM showed that they also reported a significant reduction in fatigue and increase in physical functioning (Knoop, personal communication, data available on request). Moreover, following treatment there was a significant reduction in PEM (see Stulemeijer et al, 2005, table 3).	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging

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				Can NICE please correct?	the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. There was no published data on the percentage of participants in Stulemeijer 2005, nor were there any published subgroup analyses in participants with PEM. Therefore we could not verify the information you have provided. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	211	Appendix D – Effectiveness evidence	Stulemeijer et al,2005. "Protocol outcomes not reported by the study": pain, cognitive function and sleep quality not reported on according to the review. However, in the paper (table 3) it is reported that the prevalence of pain (e.g. headache, muscle pain), impaired concentration and unrefreshing sleep decreased significantly compared to the control condition following CBT. Can NICE please correct and also amend the evidence synthesis?	Thank you for your comment. Pain outcomes (joint pain and muscle pain) and cognitive function (Checklist Individual Strength concentration sub scale and reaction time tests) have now been extracted for this study and included in the review (reported in Knoop 2007). The remaining outcomes did not meet the protocol requirement of validated outcomes.
The Royal College of Psychiatrists	Evidence Review H	226	Appendix D – Effectiveness evidence	Tummers et al, 2012: "Subgroup analysis within study: not applicable." This is not correct, there is a subgroup analysis reported. Overall there was no significant effect on physical functioning. Post-hoc analyses showed a significant increase in physical functioning following the intervention in the subgroup of patients with physical disabilities at baseline. Can NICE please correct?	Thank you for your comment. The subgroup analysis reported in the study paper was not relevant to this review, therefore this field was not applicable.
The Royal College of Psychiatrists	Evidence Review H	227	Appendix D – Effective	Tummers et al, 2012: "Seriousness indirectness of study: PEM is not a compulsory feature".	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM

Stakeholder	Document	Page No	Line No	Comments	Developer's response
			ness evidence	However, 119/123 (97%) of patients report PEM. An analysis of the group of patients who reported PEM shows that they also reported a significant reduction in fatigue and an increase in physical functioning (Knoop, personal communication, data available on request). Can NICE please correct?	reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. There was no published data on the percentage of participants in Tummers 2012, nor were there any published subgroup analyses in participants with PEM. Therefore we could not verify the information you have provided. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	246	Appendix D – Effectiveness evidence	Wiborg et al, 2015. "Seriousness indirectness of study: PEM is not a compulsory feature". However, 119/123 (97%) of patients reported PEM. An analysis of the patients who reported PEM shows that they also reported a significant reduction in fatigue and disability and an increase in physical functioning (Knoop, personal communication, data available on request). Can NICE please correct?	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendix G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. There was no published data on the percentage of participants in Wiborg 2015, nor were there any published subgroup analyses in

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					participants with PEM. Therefore we could not verify the information you have provided. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	246	Appendix D – Effectiveness evidence	Intervention: it is stated that "it is unclear whether CBT was designed specifically for CFS. This is not correct. It is clearly stated in the paper: "The intervention was based on previous work of our research group [4, 13] and included personal goal setting, fixing sleep-wake cycles, reducing the focus on bodily symptoms, a systematic challenge of fatigue-related beliefs, regulation and gradual increase in activities, and accomplishment of personal goals." This are the elements of CBT for CFS also applied in the previous work of the research group, the studies to which they refer to, more specifically nr 13, describes the intervention: Bleijenberg et al: Cognitive-behavioral therapies; in Jason L, Fennel P, Taylor R (eds): Handbook of Chronic Fatigue Syndrome. New York, Wiley, 2003, pp 493–526. Can NICE please correct?	Thank you for your comment. This section has now been amended.
The Royal College of Psychiatrists	Evidence Review H	273	Figure 33	Figure 33 shows that both Janse, 2018 and Knoop, 2008 found an improved general symptom level (Sickness Impact Profile). The term 'general symptom level' for this outcome is misleading, as the scale assesses the impact of health problems on functioning on eight domains, e.g. work or recreational activities, and not the 'symptom level'. The two studies are clustered, It is unclear why not other studies are added using the same protocol (in total 7 Dutch studies using roughly the same outcome measures, treatment protocol and inclusion criteria). This is also true for other outcomes than general symptom level, like fatigue and physical functioning. The analysis performed showed that there is no indication of significant heterogeneity, which would support the further pooling of trials testing the efficacy of CBT for CFS.	Thank you for your comment. Outcomes are agreed in the protocol before the data is extracted. Both physical functioning, quality of life and general symptom scales were critical outcomes considered equally in decision making. While we agree that the Sickness Impact Profile covers a range of functional domains, we have left it as a 'general symptom scale' as it does not change the committee's interpretation of the evidence. For clarity, the wording in the 'benefits and harms' section of the report has been amended to include specific outcomes when discussing benefits and harms, rather than just the outcome category.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				Can NICE please correct?	Only studies with the same interventions, populations and outcomes should be pooled in meta-analysis. CBT studies were analysed separately based on the delivery method (web/written, group-based, individual face-to-face), as these were considered to be distinctly different interventions.
The Royal College of Psychiatrists	Evidence Review H	273	Figure 36	Figure shows significant reduction of fatigue in three studies using the Dutch protocol. In all studies evaluated from the Dutch research group a significant reduction in found in fatigue and in all but one a reduction in the level of disability. Both are central features of ME/CFS, hence CBT can be considered a treatment for CFS/ME. However, the NICE committee concludes it is not a treatment. We argue that this conclusion does not follow from the results presented in the evidence review.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
The Royal College of Psychiatrists	Evidence review H	275	Figure 43	This is the only comparison shown for this trial for this measure of physical function, which was one of the primary outcomes of the trial, when comparing CBT vs specialist medical care. This was only shown for 134 weeks after randomisation (even though not marked as so). This is 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this data simply cannot be either an accurate or valid comparison of the efficacy of CBT vs specialist medical care. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of the therapy period (24 weeks) and at the primary end-point (52 weeks). It is highly misleading that you do not so, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence review H	279	Figure 65	This is the only comparison of CBT vs specialist medical care shown for this trial for this measure of work and social adjustment (WSAS), an important measure of disability. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison of the efficacy of CBT vs specialist medical care. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments,

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence review H	286	Figure 99	This is the only comparison shown for this trial for this measure of global improvement, comparing CBT vs adaptive pacing therapy (APT). To provide an impartial and accurate assessment of the efficacy of CBT, you should provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
The Royal College of Psychiatrists	Evidence review H	287	Figure 100	This is the only comparison shown for this trial for this measure of fatigue (Chalder fatigue scale), which was one of the primary outcomes of the trial, comparing CBT vs APT. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
The Royal College of Psychiatrists	Evidence review H	287	Figure 101	This is the only comparison shown for this trial for this measure of physical function, which was one of the primary outcomes of the trial, when comparing CBT vs APT. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence review H	288	Figure 109	This is the only comparison of CBT vs APT shown for this trial for this measure of work and social adjustment (WSAS). But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). A more reasonable conclusions would be that the benefits of CBT persisted, but the two comparison groups (SMC and pacing) caught up, possibly because of the post endpoint treatment choices of the patients. We suggest that the review is revised to correct this please	All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence review H	289	Figure 112 - 114, 122	These are the only comparisons for CGI, work and social adjustment, fatigue and physical function shown when comparing CBT and GET, even though not labelled as such. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate comparison you must do this at the end of main therapy (24 weeks) and	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). We suggest that the review is revised to correct this please	out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence Review H	300	Figure 166	Figure 166 shows the effect of CBT on self-rated improvement in adolescents in Stulemeijer et al, 2005. By changing the analytic strategy from the published protocol, this has now shifted to attract a rating of imprecision. However, Stulemeijer 2005 and Neijhof 2012 use the same treatment protocol, the same outcome measure for self-rated improvement and the same inclusion criteria. So there is no obvious reason why these should not be pooled, along with any others. Might NICE explain why this pooling was not carried out – heterogeneity seems unlikely but can of course be formally tested. Pooling is used in NICE reviews overcome exactly this issue and thus improve the information available and lead to more accurate decisions. All of this is standard NICE procedures for Guidelines.	Thank you for your comment. The outcomes are the same but Stulemeijer 2005 compares individual face-to-face CBT with waiting list while Neijhof 2012 web-written CBT with usual care (which involved rehabilitation programmes, cognitive behavioural therapy face-to-face, or graded exercise treatment)- both intervention & comparison groups in the two studies differed

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				We request that this issue corrected and the evidence synthesis updated.	
The Royal College of Psychiatrists	Evidence Review H	300	Figure 167	Figure 167 shows the effect of CBT on fatigue in adolescents. The study of Stulemeijer 2005 and Neijhof 2012 used the same treatment protocol, the same outcome measure for fatigue and the same inclusion criteria. By pooling of data one can determine the effect of CBT more precisely. However whilst the NICE committee downgraded studies because of this it did not pool data to overcome this problem. Can NICE please explain why?	Thank you for your comment. In line with the process for evidence synthesis set out in Developing NICE guidelines: the manual, only studies comparing the same interventions can be combined in meta-analysis. Considering the interventions being compared in each study, pooling was not appropriate for Stulemeijer 2005 and Neijhof 2012 as the studies examined different types of CBT and the comparison groups used also differed, the former comparing the intervention with waiting list and the latter with usual care. Looking at the results from studies examining different intervention components separately was appropriate to inform the committee about the clinical effectiveness of different types and aspects of CBT, in this case individual/face to face CBT (Stulemeijer 2005) and Web/written CBT (Neijhof 2012).
The Royal College of Psychiatrists	Evidence Review H	301	Figure 169	Figure 169 shows the effect of CBT on school absence in adolescents for Stulemeijer et al, 2005. The study of Stulemeijer 2005 and Neijhof 2012 use the same treatment protocol, the same outcome measure for school absence and the same inclusion criteria. By pooling of data one can determine the effect of CBT more precisely. However whilst the NICE committee downgraded studies because of this it did not pool data to overcome this problem. Can NICE please explain why?	Thank you for your comment. In line with the process for evidence synthesis set out in Developing NICE guidelines: the manual, only studies comparing the same interventions can be combined in meta-analysis. Considering the interventions being compared in each study, pooling was not appropriate for Stulemeijer 2005 and Neijhof 2012 as the studies examined different types of CBT and the comparison groups used also differed, the former comparing the intervention with waiting list and the latter with usual care. Looking at the results from studies examining different intervention components separately was appropriate to inform the committee about the clinical effectiveness of different types and aspects of CBT, in this case individual/face to face CBT (Stulemeijer 2005) and Web/written CBT (Neijhof 2012). No evidence was downgraded due to not pooling findings from different studies, but due to risk of bias, indirectness and

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					imprecision (uncertainty around the effect estimate, the confidence interval being wide) in the case of school absence.
The Royal College of Psychiatrists	Evidence review H	314	Figure 231	Why does this meta-analysis not include the outcome data of CGI at the end of treatment from White et al, 2011, as has been shown for Clark 2017 and Moss-Morris 2005? This would provide a more reliable test of GET than this figure alone. We suggest that the review is revised to correct this please	CGI in white 2011 is reported in a different format as opposed to the event rate of those who got better in the other 2 studies.
The Royal College of Psychiatrists	Evidence review H	314	Figure 232	This is the only comparison shown for this measure of global improvement when comparing GET vs specialist medical care (SMC) in this large trial. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment of the efficacy of CBT, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also inconsistent with how such outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided. We suggest that the review is revised to correct this please	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					. As such, we did not extract the shorter timepoints where longer follow-up was available . For outcomes where long-term follow-up was available (e.g. 134 weeks), this data was preferentially extracted in line with the review protocol, as this was the longest time point that data was available. For the remaining outcomes, 52 weeks was the longest time point that data was available, and this data was extracted. Available 24-week outcome data was not extracted as this time-point was not the longest time-point available. The review has been edited so that it is transparent to which time point outcomes reported correspond to.
The Royal College of Psychiatrists	Evidence review H	314	Figure 233	Why does this meta-analysis not include the outcome data of Chalder fatigue questionnaire at the end of treatment from White et al, 2011, as has been shown for Clark 2017 and Moss-Morris 2005? This would provide a more reliable test of GET than this analysis alone. We suggest that the review is revised to correct this please	Thank you for your comment. PACE trial study interventions ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes, including fatigue. Outcomes from Clark 2017 and Moss-Morris 2005 were reported at 12 weeks (with the exception of clinical global impression at 42 weeks in Moss-Morris 2005). Data was extracted at the longest follow-up available, as specified in the protocol for this review. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					We considered it to be a more accurate representation of the data to present the short-term and long-term data separately, and as such we made the decision not to meta-analyse long-term outcome data from the PACE trial (134 weeks) with the short-term outcome data (12 weeks) from the Clark 2017 and Moss-Morris 2005 studies. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed.
The Royal College of Psychiatrists	Evidence review H	315	Figure 234	This is the only comparison shown for this trial for this measure of fatigue (Chalder fatigue questionnaire), which was one of the two primary outcomes in this trial, for the comparison of GET vs specialist medical care (SMC). But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also inconsistent with how such outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided.	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				We suggest that the review is revised to correct this.	Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Evidence review H	315	Figure 235	Why does this meta-analysis not include the outcome data of physical function at the end of treatment from White et al, 2011, as has been shown for Clark 2017 and Moss-Morris 2005? This would provide a more reliable test of GET than this analysis alone. We suggest that the review is revised to correct this.	Thank you for your comment. PACE trial study interventions ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes, including physical functioning. Outcomes from Clark 2017 and Moss-Morris 2005 were reported at 12 weeks (with the exception of clinical global impression at 42 weeks in Moss-Morris 2005). Data was extracted at the longest follow-up available, as specified in the protocol for this review. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed.

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					Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. . We considered it to be a more accurate representation of the data to present the short-term and long-term data separately, and as such we made the decision not to meta-analyse long-term outcome data from the PACE trial (134 weeks) with the short-term outcome data (12 weeks) from the Clark 2017 and Moss-Morris 2005 studies.
The Royal College of Psychiatrists	Evidence review H	315	Figure 236	This is the only comparison shown for this measure of physical function when comparing GET vs specialist medical care (SMC) in this large trial. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also inconsistent with how such	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed.

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				outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided. We suggest that the review is revised to correct this.	Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available . For outcomes where long-term follow-up was available (e.g. 134 weeks), this data was preferentially extracted in line with the review protocol, as this was the longest time point that data was available. For the remaining outcomes, 52 weeks was the longest time point that data was available, and this data was extracted. Available 24-week outcome data was not extracted as this time-point was not the longest time-point available.
The Royal College of Psychiatrists	Evidence review H	317	Figure 246	These are the only outcomes shown for this trial for this measure of work and social adjustment for GET in comparison with specialist medical care. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				inconsistent with how such outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided. We suggest that the review is revised to correct this.	call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available . For outcomes where long-term follow-up was available (e.g. 134 weeks), this data was preferentially extracted in line with the review protocol, as this was the longest time point that data was available. For the remaining outcomes, 52 weeks was the longest time point that data was available, and this data was extracted. Available 24-week outcome data was not extracted as this time-point was not the longest time-point available.
The Royal College of Psychiatrists	Evidence review H	321	Figure 265	These are the only outcomes shown for this trial for this measure of global improvement, when comparing GET vs APT. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also inconsistent with how such outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided. We suggest that the review is revised to correct this.	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline.
The Royal College of Psychiatrists	Evidence review H	321	Figure 266	These are the only outcomes shown for this trial for this measure of fatigue (Chalder fatigue questionnaire), which was one of the two primary outcomes in this trial, for the comparison of GET vs APT. Rather repeating the point already made about the fatigue measure previously, please refer to the relevant comment above. To provide an impartial and accurate assessment of the efficacy of GET, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). We suggest that the review is revised to correct this.	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline.
The Royal College of Psychiatrists	Evidence review H	322	Figure 267	These are the only outcomes shown for this trial for this measure of physical function, which was one of the two primary outcomes in this trial, when comparing GET with adaptive pacing therapy. But the only data shown are at 134 weeks after randomisation (even though not labelled as such). This was 18 months after randomisation ceased, 18 months after the primary end-point, and 18 months after participants were free to seek any treatments they wished (which many did). So, this cannot be either an accurate or valid comparison. To provide an impartial and accurate assessment, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52	Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is

Stakeholder	Document	Page No	Line No	Comments	Developer's response
				weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review). It is also inconsistent with how such outcome data has been treated in other NICE reviews, in which either end of treatment, or early and medium outcomes, are also provided. We suggest that the review is revised to correct this	collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline.
The Royal College of Psychiatrists	Evidence review H	323	Figures 272 - 4	Finding no significant differences in non-serious adverse events, serious adverse events, and serious adverse reactions to treatment in the largest trial of GET, suggests that GET has no more evidence of harm than adaptive pacing therapy. So where is the trial evidence that justifies banning it? Might NICE please reconsider this decision?	Thank you for your comment. As with all NICE guidelines, when making decisions about interventions, the committee used its judgment to decide what the evidence means in the context of the review topic, and what recommendations can be made and the appropriate strength of the recommendation, considering many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical

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					and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).After reviewing the evidence available, together with their clinical experience, and considering the worsening of symptoms reported in the qualitative evidence, the committee concluded that programs involving fixed incremental increases in exercise are not appropriate but acknowledge that there are people who can benefit from exercise programs that are flexible, patient-led and supported by a professional. The committee recognise that each individual may differently benefit from interventions and this has been acknowledged in the recommendations that have included specific recommendations about the content of programmes involving physical activity or exercise as well as for whom such programs should be considered. In developing more specific recommendations on the content, approach and delivery of physical activity management, the committee considered the benefits and harms associated with graded exercise therapy that had been identified in the qualitative evidence and their own experiences of these types of interventions.
The Royal College of Psychiatrists	Evidence review H	323	Figure 275	These are the only outcomes shown for this trial for this measure of work and social adjustment for GET in comparison with adaptive pacing therapy. Rather repeating the point already made about the WSAS measure, please refer to the relevant comment above. To provide an impartial and accurate assessment of the efficacy of GET, you must provide this comparison at the end of main therapy (24 weeks) and primary end-point (52 weeks). It is highly misleading that you do not, particularly when you (correctly) identify 52 weeks as the duration of the study (page 14 of this review).	Thank you for your comment. Thank you for your comment. As you point out, study interventions in the PACE trial ended at 24 weeks, with the initial planned follow-up extending to 52 weeks. PACE trial authors subsequently published long-term follow-up data at 134 weeks for some outcomes. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints

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				We wish to point out that these misleading omissions occurred no fewer than 19 times in this review. We suggest that the review is revised to correct these errors.	for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. The committee note the PACE trial was only one part of the wide range of evidence considered in the decision making for this guideline.
The Royal College of Psychiatrists	Evidence Review H	354	General symptom scales (SIP)	Evidence is downgraded because of indirectness (PEM not an inclusion criteria) and imprecision. In both studies more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SIP score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Furthermore, the SIP is used in several studies using the same protocol. Pooling of these data was not done for unclear reasons, this would significantly reduce imprecision.	Thank you for your comment. Janse 2018 & Knoop 2008 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered 'direct'. The committee also agreed that

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				Can NICE please explain why?	where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. 90.4% of participants in Janse 2018 are reported to have PEM. The percentage of participants in the Knoop 2008 was not reported. Based on the above approach, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	354		Fatigue/fatigability (Checklist Individual strength - fatigue severity) in web based/written CBT - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In all three studies more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the CIS score compared to the waitlist. We argue that downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Janse 2018, Knoop 2008 & Tummers 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. 90.4% of participants in Janse 2018 are reported to have PEM. The percentage of participants in the Knoop 2008 and Tummers 2012 studies were not reported. Based on the above approach, the assessment of indirectness has not been changed.

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The Royal College of Psychiatrists	Evidence Review H	354	Appendix F – GRADE and/or GRADE-CERQual tables	Fatigue/fatigability (Checklist Individual strength - fatigue severity) in group therapy with CBT - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In the study more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the CIS score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Wiborg 2015 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Wiborg 2015 were not reported. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	355	Appendix F – GRADE and/or GRADE-CERQual tables	Physical functioning (SF36 physical functioning sub-scale) - web/written CBT) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In all three studies more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SF36 score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Janse 2018, Knoop 2008 & Tummers 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G

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					for the approach taken, the analysis and the impact on the results and interpretation of the evidence. 90.4% of participants in Janse 2018 are reported to have PEM. The percentage of participants in the Knoop 2008 and Tummers 2012 studies were not reported. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	355	Appendix F – GRADE and/or GRADE-CERQual tables	Physical functioning (SF36 physical functioning sub-scale) – group CBT - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In the group study more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SF36 score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Wiborg 2015 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Wiborg 2015 were not reported. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	356	Appendix F – GRADE and/or GRADE-CERQual tables	Psychological distress, assessed with the SCL-90 wrttten/web CBT - Evidence is downgraded because of indirectness (PEM not an inclusion criteria) and imprecision. In both studies more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SCL-90 score compared to the waitlist.	Thank you for your comment. Janse 2018 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they

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				Downgrading because of indirectness for this reason is not correct. CanNICE please explain why they did this? Furthermore, the SCL-90 is used in several studies using the same protocol. Pooling of these data was not done for unclear reasons, this would significantly reduce imprecision. Might NICE please explain why they did not do this?	agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. 90.4% of participants in Janse 2018 are reported to have PEM. Based on the above criteria, the assessment of indirectness has not been changed.
The Royal College of Psychiatrists	Evidence Review H	356	Appendix F – GRADE and/or GRADE-CERQual tables	Psychological distress, assessed with the SCL-90 group CBT - Evidence is downgraded because of indirectness (PEM not an inclusion criteria) and imprecision. In this study more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SCL-90 score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Furthermore, the SCL-90 is used in several studies using the same protocol. Pooling of these data was not done for unclear reasons, this would significantly reduce imprecision. Can NICE please explain why they did not do this?	Thank you for your comment. Wiborg 2015 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Wiborg 2015 were not reported. Based on the above criteria, the assessment of indirectness has not been changed

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The Royal College of Psychiatrists	Evidence Review H	379	Appendix F – GRADE and/or GRADE-CERQual tables	General symptom scales (self-rated improvement recovered or much better) (follow-up 5 months) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study more than 95% of patients reported PEM. Downgrading because of indirectness for this reason is not correct. Furthermore, this self-rating of improvement is used in the Neijhof et al study (2012) using the same protocol and inclusion criteria. Pooling of these data was not done for unclear reasons. Can NICE please explain why they did not do this?	Thank you for your comment. Stulemeijer 2005 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Stulemeijer 2005 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	379	Appendix F – GRADE and/or GRADE-CERQual tables	Fatigue/fatigability (Fatigue severity (CIS-20)) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria) and imprecision. In this study more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the CIS score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Furthermore, the CIS is used in the Neijhof et al study (2012) using the same protocol	Thank you for your comment. Stulemeijer 2005 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be

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				and inclusion criteria. Pooling of these data was not done for unclear reasons. Can NICE please explain why they did not do this?	considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Stulemeijer 2005 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	380	Appendix F – GRADE and/or GRADE-CERQual tables	Return to school or work - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, 87% of patients reported PEM. Downgrading because of indirectness for this reason is not correct. Furthermore, this outcome measure is also used in the Stulemeijer et al study (2012) using the same protocol and inclusion criteria. Pooling of these data was not done for unclear reasons, and should be corrected. Can NICE please explain why they did not do this?	Thank you for your comment. Stulemeijer 2005 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Stulemeijer 2005 were not reported. Based on the above criteria, the assessment of indirectness has not been changed.

Stakeholder	Document	Page No	Line No	Comments	Developer's response
					Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	380	Appendix F – GRADE and/or GRADE-CERQual tables	Physical functioning (SF36 physical functioning) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, more than 95% of patients reported PEM and an analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the SF-36 physical functioning score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Stulemeijer 2005 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Stulemeijer 2005 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	380	Appendix F – GRADE and/or	Return to school or work (School attendance (hours attended/total hours)) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria) and imprecision. In this study, more than 95% of patients reported PEM.	Thank you for your comment. Stulemeijer 2005 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further

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			GRADE-CERQual tables	Downgrading because of indirectness for this reason is not correct. Furthermore, this outcome measure is also used in the Neijhof et al study (2012) using the same protocol and inclusion criteria. Pooling of these data was not done for unclear reasons which would reduce imprecision. Can NICE please explain why they did not do this?	scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Stulemeijer 2005 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	380	Appendix F – GRADE and/or GRADE-CERQual tables	General symptom scales (follow up 6 months) - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, more than 87% of patients reported PEM. An analysis with the subgroup reporting PEM showed a significant reduction in the CBT condition of the CIS score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Furthermore, this outcome measure is also used in the Stulemeijer et al study (2012) using the same protocol and inclusion criteria. Pooling of these data was not done for unclear reasons. Can NICE please explain why they did not do this?	Thank you for your comment. Nijhof 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G

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					for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Nijhof 2012 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	381	Appendix F – GRADE and/or GRADE-CERQual tables	Physical functioning (Child health questionnaire physical functioning - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, more than 87% of patients reported PEM. An analysis with the subgroup reporting PEM showed a significant increase in the CBT condition of the physical functioning score compared to the waitlist. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this?	Thank you for your comment. Nijhof 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Nijhof 2012 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different

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					modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	381	Appendix F – GRADE and/or GRADE-CERQual tables	Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, more than 87% of patients reported PEM. Downgrading because of indirectness for this reason is not correct. Can NICE please explain why they did this	Thank you for your comment. Nijhof 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Nijhof 2012 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	381	Appendix F – GRADE and/or GRADE-CERQual tables	Return to work, school attendance 6 months - Evidence is downgraded because of indirectness (PEM not an inclusion criteria). In this study, more than 87% of patients reported PEM. Downgrading because of indirectness for this reason is not correct. Furthermore, this outcome measure is also used in the Stulemeijer et al study (2012) using the same protocol and	Thank you for your comment. Nijhof 2012 After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM

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				inclusion criteria. Pooling of these data was not done for unclear reasons. Can NICE please explain why they did not do this?	would be considered 'direct'. The committee also agreed that where this information was not available, evidence would be considered 'indirect' acknowledging the uncertainty about the study population. See the methods chapter for more information on GRADE and indirectness. Unpublished data was not accepted for this analysis. See evidence review H appendices F and G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The percentage of participants in Nijhof 2012 were not reported. Based on the above criteria, the assessment of indirectness has not been changed. Stulemeijer 2005 used individual face-to-face CBT, whereas Nijhof 2012 used web/written CBT. Studies using different modalities of CBT were not combined as the committee considered these interventions too different to each other.
The Royal College of Psychiatrists	Evidence Review H	450		S Knoop et al, 2007. The effect of CBT for chronic fatigue syndrome on self-reported cognitive impairments and neuropsychological test performance. JNNP 78(4):434-436) was excluded because the '*data were not useable'*. This is not correct. The data presented are from RCTs testing the efficacy of CBT for ME/CFS The analysis of these data show that (self-reported) cognitive impairment, a characteristic symptom of CFS/ME and seen by the NICE committee as a relevant outcome significantly decreased following CBT. Can NICE please correct?	Thank you for bringing this to our attention. Data for the outcomes CIS-concentration sunscale and reaction time tests for the adolescent population reported in the study (relating to included study Stulemeijer 2005) have now been included in the review. See evidence reviews G and H. Note we have not included the self-reported cognitive impairment outcome as this is not a validated scale as specified in the review protocol. Additionally, we have not included data from the adult population reported in the study as this relates to a study excluded for having an incorrect population (see excluded studies table in evidence review H).
The Royal College of Psychiatrists	Evidence Review H	450		Study of Knoop et al, 2007. Is CBT for chronic fatigue syndrome also effective for pain symptoms? Behaviour Research and	Thank you for highlighting this. This study has now been included in the review and pain outcomes extracted.

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				Therapy. 2007; 45(9):2034-2043) was excluded because 'data were not relevant'. This is not correct. The study reports on a significant reduction in pain following CBT in an additional analysis of the adolescent study of Stulemeijer et al, 2005, an RCT comparing CBT to a waitlist condition. The proposed NICE guideline indicates that pain is a relevant outcome of interventions for CFS/ME. Can NICE please correct?	
The Royal College of Psychiatrists	Evidence review H	452		Given however that the threshold was set at 90%, the Committee need to reconsider the decision to reject completely the Prins et al 2001 Lancet CBT trial, on the grounds that it included some participants that did not fulfil the criteria for ME/CFS (CDC). This is true. However, as the authors reply to the Lancet showed (https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(01)05423-X.pdf), 93% of the participants fulfilled CDC Criteria, and as the PI of the trial also confirms, 99% of the participants had PEM (Prins, pers communication). Even without that information, the trial should be included using the threshold set by the review. Will NICE please reconsider that decision to ensure that they did take account of all the relevant evidence, and use the recognised statistical methods to look for heterogeneity.	Thank you for your comment. This review only included people diagnosed with ME/CFS. The committee agreed it was important that only studies where all participants were diagnosed with ME/CFS should be included in this review as they considered that people without ME/CFS are likely to react differently to interventions compared to people with ME/CFS, and this could skew the results. The committee did not set a 90% threshold. Only studies where 100% of study participants were diagnosed were included. Prins 2001 had a population which included people with idiopathic chronic fatigue (7% of the study population), and results were not reported separately for those diagnosed with ME/CFS, therefore this study was excluded. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing cut-off percentages for populations for NICE reviews and each committee has to consider the degree to which this may impact

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					the interpretation of the results within the context of the particular condition being assessed.
The Royal College of Psychiatrists	Evidence Review H	452		Prins et al, 2001 was excluded, reason: Not review population; also includes ICF. This is one of the largest studies thus far testing the efficacy of CBT for CFS/ME. Of the included patients, 94% met all CDC criteria. This has been published in a letter to the Lancet, see attachment. The subset of patients who fulfill all CDC criteria showed similar positive effects of CBT compared to support groups and natural course with respect to fatigue severity and level of disability (Knoop, personal communication, data available on request). The inclusion of this large study could influence the evaluation of the efficacy of CBT for CFS/ME. Furthermore, 99% (275/278) of patients report Post Exertional Malaise (PEM), a cardinal feature of ME/CFS according to proposed guideline, further underlining the relevance of the study of Prins et al. A subgroup analysis with the patients reporting PEM showed that following CBT, fatigue severity and level of disability significantly decreased following CBT compared to the control conditions (Knoop, personal communication, data available on request). Can NICE please correct?	Thank you for your comment. This review only included people diagnosed with ME/CFS. The committee agreed it was important that only studies where all participants were diagnosed with ME/CFS should be included in this review as they considered that people without ME/CFS are likely to react differently to interventions compared to people with ME/CFS, and this could skew the results. The committee did not set a 90% threshold. Only studies where 100% of study participants were diagnosed were included. Prins 2001 had a population which included people with idiopathic chronic fatigue (7% of the study population), and results were not reported separately for those diagnosed with ME/CFS, therefore this study was excluded. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing cut-off percentages for populations for NICE reviews and each committee has to consider the degree to which this may impact the interpretation of the results within the context of the particular condition being assessed.
The Royal College of Psychiatrists	Evidence Review H	452		The Study of Severens et al, 2004, an economic evaluation of the RCT reported on in the publication of Prins et al, 2001 was excluded: "HE analysis of excluded study (Prins 2001). However, the study of Prins et al consisted for 93% of patients meeting all CDC criteria and 99% of patients reported PEM. The inclusion of	Thank you. The review protocol required that patients in a study had to have ME/CFS in order to be included. Prins et al 2001 and Severens et al 2004 did not meet this criterion and so were excluded.

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				this study could influence the economic evaluation of CBT for CFS/ME and should be taken into account. Can NICE please correct?	
The Royal College of Psychiatrists	Evidence Review H	453		Van der Schaaf et al 2015 was excluded because it was a protocol paper. The study is completed and data can be made available by the Dutch research group on request (Knoop, personal communication). Analysis of unpublished date that CBT compared to waitlist is followed by a significant decrease of fatigue and disability. Can NICE please correct?	Thank you for your comment. For this review we could only include papers that were published within our initial and re-run search dates. We identified the trial registry page for this trial in our search (https://www.trialregister.nl/trial/4122) but we could not locate any published data.
The Royal College of Psychiatrists	Evidence review H	518 onwards	Appendix D page 518 onwards; Evidence reviews for information, education and support for people with ME/CFS and their families and carers;	The reviews of the qualitative evidence for effectiveness (Review H), and the qualitative evidence on information/education/support (Review A) included over 40 studies. 10 had been diagnosed with recognised criteria for ME/CFS, usually as part of a trial. However, for the rest there was an extraordinary diversity of different criteria or none at all. The commonest group (12) had been "confirmed diagnoses by a medical practitioner" using unknown if any criteria, five just had self-report of a medical diagnosis, four had self-report of having ME, and the rest either gave no information or it was unrateable (ex "people with ME"). Similar limitations applied to the study of severely affected (Appendix 2, page 41, line 16), in which "we relied on respondents to attest to their ME/CFS. This is common practice in this field, given it is often too costly and time consuming to medically screen every patient for a confirmatory diagnosis". So no attempt was made to see if any exclusionary diagnoses applied, that any known criteria were fulfilled, or whether what the committee regarded the mandatory symptom of PEM was present. The committee listed a long list of caveats (page 45), concluding that "this was taken into account when considering the findings of the research", but we could not find any	Indirectness in the qualitative studies Thank you for your comment. The committee acknowledge there are methodological limitations including limitations in the recruitment strategy across various studies which may limit the applicability of the findings to the population of interest. These have been assessed in line with NICE methods, using the GRADE CERQual approach. After considering stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed to revisit the evidence for the intervention reviews, further scrutinising the information on PEM reported in the studies and its impact on the relevance or the indirectness rating of qualitative or quantitative findings they contribute to respectively and in turn on the overall assessment of confidence in the findings (qualitative)/ quality assessment (quantitative). As part of this the committee agreed that any evidence with a population ≥ 95% with PEM would not be downgraded for concerns over relevance/ indirectness if additional concerns regarding applicability were not present. Studies where < 95% of participants had PEM, or where the percentage of participants

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			Evidence review A	corroboration that this actually happened in practice, such as agreeing that this did reduce the confidence with which the committee stated their recommendations – but there were plenty of indications that the opposite was true where it fitted with the committee's own experiences. Either "indirectness" matters, or it doesn't. What is unacceptable is the inconsistent implication that it matters in clinical trials but not in qualitative studies. Could NICE please provide a view on this matter?	with PEM was not reported would be downgraded for concerns over relevance. See Evidence review H Appendix G on 'PEM-reanalysis' for the approach taken, the analysis and the impact on the results and interpretation of the evidence. The committee agreed the requirement of PEM was particularly important in the studies evaluating interventions as they considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and were able to take this into account in decision making through revisiting all evidence relevant to interventions following the PEM reanalysis. The changes this has made in the confidence of the qualitative findings have been incorporated throughout the relevant sections of Evidence review G.
The Royal College of Psychiatrists	Evidence Review H	668		Heins et al, 2010 (ref 322) is an additional analysis of three RCT's testing the efficacy of CBT for CFS and reporting on possible detrimental effects of CBT. This study is not discussed in the clinical effectiveness section for unclear reasons. This study shows that CBT in these three trials has no detrimental effects compared to control conditions which is a highly relevant finding in the light of the discussion on possible negative effects of behavioural interventions (Heins et al. Psychotherapy and Psychosomatics. 2010; 79(4):249-256). Can NICE please correct?	Thank you for your comment. After reviewing the evidence available, together with their clinical experience, the committee agree that although CBT is not curative for ME/CFS, it is a useful intervention to help people manage ME/CFS symptoms and live better and that it should be available to all people with ME/CFS. A recommendation has been made to offer CBT to ensure this will be the case. The Heins study was not excluded from the quantitative review but it was not identified in the systematic searches conducted for it to allow us to consider it for inclusion at that stage. It was identified from the evidence submitted within the call for evidence that accompanied the qualitative experiences of interventions review. Evidence submitted within this call for evidence was assessed for inclusion in the qualitative evidence review in addition to the evidence identified in the systematic searches following the same process of assessment against the review protocol.
The Royal College of Psychiatrists	Evidence Review I	024	023	"*Some of the committee members working in specialist teams noted they had 1- 2-hour initial appointments with people with suspected ME/CFS and access to professionals who had the time to develop a personalised management plan.*"	Thank you for your comment. The length of the initial meetings has been added to the committee descriptions of ME/CFS specialist teams in Evidence review I-Multidisciplinary care.

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				Those of our members who work in CFS Services have commented that this standard practice for their services as well, a 60 to 90 minute initial assessment followed by an equally lengthy and personalised assessment for treatment, including GET if desired. We suggest that this should be a positive recommendation of the Committee and/or be part of any description of what good should and does look like.	
The Royal College of Psychiatrists	Evidence reviews G (and D decision spilt between both sections)	052	004	The decision to downgrade the on every trial using CDC or Oxford criteria is also inconsistent with the Evidence Review's findings on diagnostic criteria – *"Diagnosis Recommendations 1.4.1 to 1.4.3" "The committee made a recommendation for key symptoms based on the evidence review of the current diagnostic criteria but no one criteria was agreed to be better overall*" And likewise, in Evidence review D: diagnosis 1.2 Suspecting ME/CFS: *""The diagnostic criteria have not been evaluated in terms of their measurement validity and accuracy in diagnosing ME/CFS. Without a biomarker it is not possible to definitively know if a person has or does not have ME/CFS. Without such a reference standard (or 'gold standard') it is not possible to assess the measurement validity of the different criteria".* But despite finding a lack of superiority of any one set of criteria, the committee made up their own criteria de novo, without supporting scientific evidence. This was an unusual decision in its own right for a guideline, but the committee then went on to use this judgement to justify downgrading the majority of the available clinical trials from their evidence review and to exclude Cochrane reviews. The College have never encountered such a set of decisions and find it hard to understand who the committee could come to such conclusions.	Thank you for your comment. Three Cochrane reviews were excluded from our review, but they were not excluded because of the diagnostic criteria used. Reasons for exclusion are highlighting below and the review has been edited for clarity (see excluded studies sections in evidence review G and H). Larun 2017: This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures,

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				Can NICE cite another similar example from any guideline of a similar decision? Furthermore, it does not seem reasonable in such a state of uncertainty to put so much importance on any single symptom or any single criteria in the absence of any reference standard, biomarker or gold standard. We are aware that this has happened in the past, for example when a gene discovery is made that transforms the entire diagnostic landscape, and forces a reconsideration of previous knowledge. This is not such a moment.	and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. Price 2008: This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. Adams 2009: This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full)
The Royal College of Psychiatrists	General	General	General	1. The Committee created a new definition of ME/CFS on the grounds that they felt it best described the condition. They "acknowledged that this judgement was made in	Thank you for your comments. *1.PESE/PEM*

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				the absence of formal measures of accuracy". They decided, in the absence of strong supporting evidence that the one symptom in their new definition, post-exertional symptom exacerbation (PESE), was the essential feature of ME/CFS and that they would downgrade any trial which used diagnostic criteria that didn't list PESE as a requirement for inclusion, as being poor quality due to population indirectness. But there was no evidence that the small differences they made to the existing and widely used criteria made any difference to outcomes of treatment. The Review itself concluded that there is no superiority of one definition over another and no "Gold Standard". 2. They then used this new untested approach to discredit over 90% of the available evidenceon the treatment of ME/CFS. That a CBT trial that was rated as the highest quality in 2007, with a score of 18/20, could now be given the lowest rating, requires some explaining. 3. The committee excluded any evidence from Cochrane Reviews, which are a standard resource for NICE Guidelines with unconvincing reasons. One reason is again "indirectness", which can be tested and in our opinion would have been found wanting if it had been. The other is that that the Cochrane Reviews had not included all of what the Review had decided were critical outcomes, the outlier seemingly mortality. They would have known that clinical trial data from ME/CFS would not have included mortality as an outcome – the power calculation would give an impossible sample size. Large mortality studies already do exist, showing for example a tragic increase in suicide in those seen in a secondary care setting – Cochrane would have added nothing to this. We find the stated reasons for excluding Cochrane implausible. There are ways of testing indirectness, and the absence of mortality data or	It is commonly agreed that people with ME/CFS can experience PEM* after activity. The committee note it is the combination and the interaction of the 4 symptoms in the criteria, particularly with the addition of PEM, that are important in the diagnosis of ME/CFS. As such PEM is essential in the diagnosis of ME/CFS. See evidence review D- Diagnosis for the committee discussion of the evidence. *To note, after considering the comments made by stakeholders about the potential for misunderstanding the committee agreed to change *Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM).* The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. *2.Methods* All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. Published date: 31 October 2014 Last updated: 15 October 2020. The last guideline was published in 2007 when GRADE was not implemented in NICE guidelines to evaluate the quality of the evidence. The score you refer to in the 2007 guideline is the validity score for a study . This is similar to critical appraisal assessment, the GRADE rating assesses the quality of the evidence for each outcome (not the study) and takes into account other factors. *PEM and Indirectness* After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they

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				indeed any particular outcome is a red herring. Neither would have been a barrier to the Cochrane Reviews adding useful information, especially given the Review's reluctance to use data pooling. 4. The committee decided that the clinical trial data should be analysed according to the longest time point available, ignoring outcomes at earlier trial endpoints and using long term outcome data even if patients were no longer in randomized groups. This is misleading. 5. The committee appears to have given excessive influence to the question of lack of blinding (which is an acknowledged potential source of bias which hundreds of NICE Guidelines have had to take into account for years, without excluding such evidence). and self-reported outcomes. We regard the latter not as a weakness, but a strength, respecting the centrality of the patient experience, in this and many other areas of health and illness, and is also something which NICE methodologies consider and did consider in this case. Despite that, the additional importance that the Committee paid to this has meant that the 3,659 ME/CFS sufferers who participated in the trial they downgrade have had their own self-reported experiences, as recorded in the assessments they underwent and the measures they completed, ignored or devalued. 6. The effect of these decisions was that there was no longer much useful evidence to base any recommendations on. The committee has filled the gaps with their own views and personal experience, which we felt in the end undermined the NICE's stated aim to create a methodologically rigorous guideline. 7. These methodological errors have produced a guideline that contradicts the recommendations of the previous Guideline, the Cochrane reviews on the treatment of	agreed that any evidence with a population > 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence. 3.Cochrane reviews Three potentially relevant Cochrane reviews were identified but were not included in this review due to differences in the review protocols and methodologies. All included studies within these reviews were cross-checked for eligibility for inclusion in this review. Exclusion reasons are now clarified below and in the report. **Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions

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				ME/CFS, the general principles of rehabilitation for fatigue in the context of neurological disease and the general principles of long-term condition management. This will be baffling for clinicians and potentially harmful for patients. 8. The guideline is currently so methodologically poor that that it is difficult to have any confidence in its conclusions. That may be a blessing in disguise, because if its principal conclusion stands - this is an illness for which there is no treatment - then already scarce resources will most likely be moved towards different areas where there are treatments available. 9. The College also notes that the recommendations are in sharp contrast to those of the draft review for the management of chronic pain – which as the Review notes is a serious problem for many ME/CFS sufferers. But whilst one review recommends exercise therapies and psychological treatment including CBT, the other bans or downgrades it. This inconsistency will cause major problems for professionals and patients. 10. Our faculties also expressed disquiet on the issue of choice. No one can be forced to receive CBT or GET, which are both collaborative therapies. We are concerned that banning GET and restricting CBT would mean that those ME/CFS patients who want these treatments would be denied the opportunity to receive them. 11. The College welcomes the strong voice of patients in the review and that clinicians learn from criticism. However, we feel it should reflect the totality of the patient experience and we are not sure that has been achieved. For example, the Committee might have benefited from hearing more from patients who have recovered.	of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update. **Price 2008:** This Cochrane review looked at CBT versus usual care or other interventions in adults with 'CFS'. The main reasons for exclusion are as follows: Studies with mixed populations where at least 90% of participants had a primary diagnosis of CFS were included. The committee agreed it was important that all participants in included reviews were diagnosed with ME/CFS. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, pain, sleep quality, activity levels, exercise performance, and mortality. It is also worth noting that Cochrane has stated that this review is no longer current and should not be used for clinical decision making. **Adams 2009:** This review did not include any studies, as no studies that met all of the inclusion criteria were identified. An updated version of this review published in 2018 was withdrawn from publication. (https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006348.pub3/full) 4. Time points Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical

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				12. The College is also of the view that some clinical disciplines were not adequately represented. Why was there no specialist in rehabilitation, surely a core discipline when so much of the deliberations of the committee were focussed on this topic? Where was the voice of those with years of experience running large multi-disciplinary teams? Indeed, amidst all the talk of multi-disciplinary teams, some disciplines were conspicuous by their absence. There were numerous instances in the report where it seems as if active efforts were made to marginalise mental health and those who work in it, such as psychology and psychiatry– for example the remarkable absence of any mention of depression (reduced to one item containing external links) or other important comorbidities, the absence of any acknowledgment that psychiatric disorders are a major differential diagnosis, why ME/CFS seems to be the only long term condition in which psychiatric comorbidity is mentioned only once and that being a link to another guideline, and finally why professionals practicing CBT are considered to be treating patients in other areas of medicine, but not ME/CFS.	practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. <u>5. Blinding</u> No evidence has been excluded that met the inclusion criteria in the protocols. All NICE guidelines follow the process for evidence quality assessment set out in Developing NICE guidelines: the manual. Appendix H (of the manual) gives examples of checklists that can be used to assess risk of bias or quality of studies when developing guidelines. This guideline has used the Randomised Controlled Trial: Cochrane RoB (2.0) checklist to assess risk of bias and GRADE to assess the quality of the evidence for each outcome. These assessments are detailed in Evidence review H: Non pharmacological appendices. The committee strongly agree that the opinions and experience of people with ME/CFS are a strength and to ensure the voice of people with ME/CFS was heard in the guideline xx qualitative reviews- 1 on the experience of interventions, 4 calls for evidence and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature were included. In addition the committee had 5 patient/carer representatives. 6.<u>No useful evidence base</u> No evidence has been excluded that met the inclusion criteria in the protocols.

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					When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). 7,8. Methodological errors and methodologically poor Please see responses to points 1-6 for an explanation of the methods used in NICE guidelines and how they are applied in this guideline, we disagree the guideline is methodologically poor and that there are methodological errors in the guideline. 8. No treatment After taking into consideration the stakeholders comments on the use of treatment in the recommendations alongside cure the committee agreed to delete 'treatment'. The committee recognised that in this context this could be misunderstood as no treatment available for symptom management. 9.Chronic pain guideline The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population '

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					chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account. 10. Choice The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. Unfortunately, some people with ME/CFS have reported experiences to the contrary and have reported pressure to undertake or continue a treatment they considered was unhelpful (Evidence reviews A and C). CBT and GET The management sections of the guideline include recommendations: • to support people with energy management

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					- to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. - to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. 11. Guideline reflecting all people with ME/CFS When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.).

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					In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. 12.Committee composition The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. A clinical psychologist with experience in delivering CBT to people with ME/CFS was recruited to the committee. In addition, Dr Husain was invited to give his reflections on the different models of multidisciplinary care, including team composition, for people with ME/CFS (Appendix 3- Expert testimonies). In the discussion section of Evidence review I- multidisciplinary care the committee have acknowledged the historical context in the variation in how ME/CFS services are led in the NHS and added further text about the composition of ME/CFS specialist teams 12.Mental health comorbidities

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					The committee have revised the list of differential diagnosis and added, mental health conditions: anxiety, depression or mood disorders.
The Royal College of Psychiatrists	General	General	General	Many of our members expressed significant disquiet that so many decisions simply reflected the committee's opinions. Our members, who have extensive clinical experience with ME/CFS, running services that have been able to demonstrate positive outcomes and high satisfaction, had very different opinions to those expressed here. We argue that the apparent consensus reached by this committee is a limited one and one only achieved by ignoring evidence. If NICE Guidelines are to be trusted in a contentious area such as this one, they must acknowledge the diversity of opinion and strive to achieve genuine consensus around the available evidence. Does NICE believe that this has been achieved here?	Thank you for your comments No evidence has been ignored. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. Please see the heading below 'committee composition' for further detail. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will take into account many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Committee composition

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					The committee composition was agreed during the scoping phase as appropriate for the expertise for the guideline scope. Great care was taken to ensure the committees was formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. The committee membership does reflect the multidisciplinary approach to treating ME/CFS and includes medically qualified clinicians and allied health professionals who lead and work in specialist ME/CFS services. In addition, Dr Husain was invited to give his reflections on the different models of multidisciplinary care, including team composition, for people with ME/CFS (Appendix 3- Expert testimonies). In the discussion section of Evidence review I- multidisciplinary care the committee have acknowledged the historical context in the variation in how ME/CFS services are led in the NHS and added further text about the composition of ME/CFS specialist teams
The Royal College of Psychiatrists	General	General	General	It must be very unusual for a guideline to start with two recommended treatments, end with none, and conclude that the illness is incurable after only a few weeks of symptoms. Is NICE aware of any precedents here?	Thank you for your comment. The guideline updates the NICE guideline CG53 published in 2007. This includes updating the evidence and it is not unusual for updated guidelines to have different recommendations based on the new evidence compared to the one they have updated.
The Royal College of Psychiatrists	General	General	General	The committee argues that adverse events occurred "especially when GET is poorly implemented" (Evidence Review G , p344, 35). The College agrees with this statement and notes this likely explains why there was little evidence of adverse events in the controlled trials, which by definition were being delivered by centres with experience of GET, when compared to survey reports from patients treated by unspecified services and individuals.	Thank you for your comment. The committee agree that any care to people with ME/CFS should be delivered by health and social care professionals that have training relevant to their role and in the case of specific interventions, such as physical activity and exercise programmes these are overseen by a physiotherapist working within a ME/CFS specialist team. As you note in addition advice is given

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				We suggest that the reasonable response to these concerns about delivery of treatment is to take steps to ensure that GET is not delivered poorly. Less contentious recommendations, such as improving standards, training or registration systems, would have allowed those patients who wished to try such approaches. It could be recommended that, with informed consent, patients could access services that follow the standards that, perhaps ironically, the committee did outline in various parts of the Guidelines (no fixed incremental increases, individualised assessments and so on), all of them recommendations with which we heartily agree. Why was this option, which we think would have been both much more evidence-based and more likely to achieve a broader consensus, not considered?	on what a physical activity or exercise programme should look like for someone with ME/CFS. For the specific committee discussion on physical activity including graded exercise therapy see the committee discussion in Evidence review H- non pharmacological management.
The Royal College of Psychiatrists	General	General	General	Stigma - The College would also like to draw attention to the general issue of how the Review has approached the field of mental health in general and how it has inadvertently perpetuated stigma. There are many places in which it is easy to form the impression that that the committee has operated in a dualistic way; implying there is a hierarchy of illness with mental illness seen as less important. This does not reflect the reality of clinical practice and the experience of illness. It has not challenged examples of misunderstanding and mythology around mental disorder, and on occasion perpetuated them. There is an assumption that interventions such as CBT cannot be considered a treatment, unlike for example pharmacological interventions – the reluctance of the committee to accept that some people can recover after CBT is palpable. There is even a contrast in the way the Review responded to the expert witnesses, up to and including a misrepresentation of what the psychiatrist witness actually said.	Thank you for your comment. The committee disagree they have taken a dualistic approach to the guideline. A holistic personalised approach to the assessment and the management of ME/CFS is recommended throughout the guideline. The committee agreed to make some edits to the recommendations to the guideline and hope this has addressed your points and added some clarity for readers. In summary the edits to the points you make are: • Replacing 'comprehensive clinical history' in section 1.2' suspecting ME/CFS' and full 'history' in section 1.5 Assessment…by a ME/CFS specialist team' with medical assessment with physical and mental health included. • Recommendation 1.6.10 includes the importance of assessing and meeting the mental health needs of families and carers. • Management plan has been edited to 'care and support plan' in line with personalised care and support plans

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				We were struck by the extraordinary way in which depression has been side-lined. It is mentioned just once in the recommendations, and that is to link with other NICE Guidance. To ignore depression, and other relevant psychiatric disorders, in the differential diagnosis, is extraordinary, and potentially dangerous. As it stands we think that ME/CFS will be the only long term condition in which it is acceptable to consign a key morbidity, more not less common than in other chronic illnesses, to just a link? Does NICE regard this as appropriate?	https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.) • the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders. As you note these are already included in the guideline under managing co-existing conditions. *Treatment and cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters. *Prognosis* After considering the range of stakeholder comments on this bullet point it has been edited slightly to,' varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.' There is particular reference to children and young people. This is to reflect the experience of all people with ME/CFS. *Misrepresentation of Dr Husain*

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					Dr Husain's written statement is in Appendix 3 _Expert testimonies and Dr Husain's observations on mood disorders are included. There is no reference to emotional well-being in Dr Husain's written summary or in the summary of his testimony in Evidence review I_ Multidisciplinary Care. After further contact with Dr Husain the summary of his presentation to the committee in Evidence review I has been edited to include, 'Dr Husain commented that it is important to ensure other causes of fatigue are considered and to assess for mood disorders, such as depression which are common in long term conditions'.
The Royal College of Psychiatrists	General	General	General	We are now going to take a detailed look at several methodological issues that we think have had a significant impact on the conclusions reached by the Committee. The first is the issue of "indirectness" and the decision taken to downgrade all the clinical trial evidence used in the previous review, and nearly all the new evidence that has emerged since then	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. Published date: 31 October 2014 Last updated: 15 October 2020. The last guideline was published in 2007 when GRADE was not implemented in NICE guidelines to evaluate the quality of the evidence. *PEM and Indirectness* After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness in the evidence. As part of this they agreed that any evidence with a population $\geq$95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	General	General	General	We have a general problem in the way in which qualitative evidence has been used, particularly when it comes to adverse effects. Overall, we accept that such evidence might identify a signal, but that will rarely be sufficient to come to a conclusion on	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline

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				whether an intervention should be withdrawn. For that we need evidence from quantitative studies such as RCTs or observational studies if the possible harms are rare. In guideline development, qualitative evidence can of course be useful (but still combined with quantitative evidence) for assessing how patients consider the relative importance of outcomes (their values and preferences – e.g. how important are specific beneficial outcomes versus potential harms), and issues related to acceptability and feasibility of interventions. Again, views need to be sought not just from those who have negative experiences, but positive experiences as well, and other stakeholder views should also be looked for. Qualitative evidence synthesis also requires reflexivity - the authors, ie the Committee, need to reflect on their experience in this area, take account of what are called "priors"- ie the position they brought to the table before they sat down to read the evidence, and demonstrate that they have considered how their positionality may influence the results obtained. Overall, we don't think that this happened. Could NICE comment please?	was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. The process for quality rating used in NICE guidance is an internationally agreed process and it is not unusual for evidence to be graded as low or very low quality. This does not mean it cannot be used to make recommendations but affects the strength of recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The balance of perspectives and experiences on the committee ensures that reflexive practice is inherent in its decision making. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality

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					considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The use of qualitative evidence in this guideline has been no different to other NICE guidelines where there is limited quantitative evidence. *Harms/ adverse events* The committee agree there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. As you note this ideally takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention,. patient experience is invaluable. The Cumberlege review 2020 has highlighted the failures and impacts on lives when this does not happen.
The Royal College of Psychiatrists	General	General	General	To assist the review staff and the reader, we include the list of all the incorrect and misleading comparisons at the end of the document.	Thank you for your comment.
The Royal College of Psychiatrists	Guideline	General	General	The Royal College of Psychiatrists welcomes NICE updating their guidance on ME/CFS. The College recognises that ME/CFS can be a highly disabling and distressing illness and for many sufferers it is a chronic condition. The College recognises that the cause of the illness is unknown and that this fact may contribute to disbelief and stigma for patients. The College has considerable experience of stigma and understands its malign impact on health and wellbeing. We also know that misunderstandings and disbelief by health professionals has also impacted on health and wellbeing of sufferers. But our own	Thank you for your comments. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be

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				experiences also confirm that this can be avoided or overcome when health professionals have sufficient knowledge, experience, skills and in particular time to spend with patients with ME/CFS and follow the general principles of patient centred care and co-production that this College promotes. The College recognises that many patients have had bad experiences of the only two therapies recommended in the 2007 Guidelines, namely GET, and to a lesser extent CBT. This may have arisen from poor practice, underfunding, and lack of support or training for health professionals, as the Review confirms. We also note that from the evidence and our own experiences that some therapists think they are delivering GET or CBT when they are not, and so some patients are led to believe they are receiving GET or CBT when they are not. This can lead to poor practice and poor outcomes. We agree that there needs to be improvement in the average patient experience, and that the Guidance does speak to this in places. We believe the best way to achieve this is by removing what is bad (poor practice) but without at the same time removing what is good, and again the evidence within the Review attests to the existence of the good as well as the bad. Unlike the review we do not think it is beyond the bounds of possibility to achieve this. This is not the view of the Review, as it recommends banning one treatment (GET) and weakening another (CBT). We feel this not the best way forward. The Review's recommendations are that patients be informed that they have an illness for which there is no cure and no treatment. A bleak prospect indeed, but one with which we strongly disagree. We agree with the Review that more and better services are needed for what is still a neglected part of health care but the	covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *Management of ME/CFS* The management sections of the guideline include recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or programme into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and reduce the distress associated with having a chronic illness and are options for part of the care and support plan where appropriate and chosen by the person with ME/CFS. To

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				consequences of the Review's recommendations make it more likely that there will be disinvestment, and not investment, in much needed services. There are however areas of common ground. We welcome the recommendations that health professionals provide patient-centred care, including creating the time to build trust, carry out a thorough assessment, illness validation, and giving a clear diagnosis of ME/CFS when appropriate. Evidence confirms that many services already do work to such standards, but not all. This could easily be improved. The College fears that these aspects of good practice may be undermined if diagnosis is also to be followed by a statement that there is no cure and no treatment for the illness, together with what we consider to be an unbalanced emphasise on the dangers of exercise and the benefits of rest. All of this may have the unintended consequence that health professionals may become more reluctant to make the diagnosis, fearing that harm may result. Looking "under the bonnet" of the Guidelines, we were disappointed though to see that some of the recommendations were far from sturdy. In our opinion the methods, evidence reviews and interpretation of available data fell below what we have come to expect. We detail our specific concerns in the NICE specified manner below and also provide an introductory note to aid interpretation of our critique.	accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. See evidence reviews G and H for the evidence and the committee discussion on these recommendations. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
The Royal College of Psychiatrists	Guideline	General	General	The College agrees that too many people have had bad experiences particularly when specific therapies such as GET are applied inappropriately and with lack of supervision. We	Thank you for your comment.

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				recognise that there are quality control and training issues that must be addressed. The College is however also aware that many patients have benefited and more have welcomed the opportunity to receive rehabilitative therapies. It is concerned that the patient voice on this complex and at times emotive topic is limited to only one perspective. Further the College is aware that many clinical services have systematically collected patients' experience data and that it is frequently reported as a secondary measure in clinical trials. We suggest that too little attention has been paid by the committee to these differing perspectives. Given the lack of alternate treatments available, the College suggest NICE should ensure that account is taken of the full range of patients' views and seek to use systematically collected patient opinion where available, before making a decision depriving some patients of their only treatment option. The College would be happy to assist in the curating of such data.	The committee membership had a broad range of professional and personal knowledge about the different experiences of people with ME/CFS and this was discussed and considered at all stages of the decision making. The committee recognise that there is little representation in the literature of people who have recovered from ME/CFS and the committee would welcome research and publications in this area as this can only further inform the care and support of people with ME/CFS. In conclusion, the committee have modified some of its recommendations in response to stakeholder feedback. They assert that this guideline is based on the broad evidence base and are confident that commissioners will demand these services.
The Royal College of Psychiatrists	Guideline	General	General	The College was concerned that the general uncritical endorsement of an approach based upon staying within a so-called "energy envelope" is at odds with the highly critical approach taken to other therapies. For example, most specialist programmes regard the best approach in similar circumstances as one of so-called activity pacing aimed at increasing meaningful activity rather than symptom avoidance, and yet this idea is not even outlined as an alternative possibility. No mention is made of the absence of evidence for the "energy envelope" approach. Prolonged inactivity – even at the level of sedentary behaviour, much less bedrest - is known to be harmful and yet no mention is made of this obvious point as a counter to the extended	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the

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				discussion of the harmful effects of CBT or graded activity reported by some patients. It is particular striking that whilst mention is made of the importance of examination for the complications of excessive rest such as the presence of bed sores, contractures and DVTs (Evidence Review G, page 338) this is no associated consideration of the well-known dangers of sedentary behaviour Furthermore, inactivity is known to be associated with reduced wellbeing and physical worsening. Exercise is recommended in every age group and for all chronic conditions and is the fundamental basis for rehabilitation in every chronic neurological disease. The art of rehabilitation is managing the activity at a level that the patient can safely cope with and progressing it gently. The extreme position adopted within the guideline that all exercise is bad is a fundamentally counter-intuitive scientific proposition. The College would like to enquire if NICE have conducted a risk assessment of their liability for potential adverse outcomes with regard to this aspects of their guidance?	commissioned report on children and young people) and their own experience. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. Prolonged inactivity After considering the stakeholder comments the physical maintenance section has been edited to add some clarity for readers. In summary the edits are: • The section has been renamed to physical functioning and mobility • text has been added to the recommendation to clarify this is about strategies to maintain and prevent the deterioration of physical functioning and mobility • text has been added that this should be small amounts and throughout the day • strength and endurance has been replaced by muscle function *Physical activity and exercise*

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					After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. • the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity and exercise programmes. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. See evidence reviews F and G Non-pharmacological management for further information on physical activity and exercise including the committee discussion on the trade-off between benefits and harms in the evidence and the recommendations.

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					Throughout the development of the guideline the committee considered the risks and benefits of making each recommendation, this included the potential for any adverse outcomes. These deliberations are outlined in the committee discussion section of the evidence reports.
The Royal College of Psychiatrists	Guideline Evidence Review D + G	General	General	The relationship between ME/CFS and depression, just taking one example from the field of psychiatric disorders, is one of the most studied and best documented areas that exists in the literature. Starting over 30 years ago, and continuing to the present day, we know the following. Depression and the other mental disorders are very important at many levels. 1. Depression and other mental disorders are the commonest alternative diagnosis to be encountered in primary care/secondary care. When it comes to differential diagnosis in primary care, a mental state examination has a higher yield than any of the tests listed above. So for example "prolonged fatigue/neurasthenia syndromes" are common in Australian primary care settings, and are commonly associated with current depressive disorders. https://onlinelibrary.wiley.com/doi/abs/10.5694/j.1326-5377.1996.tb122199. Or in UK Primary care 72% of those presenting with chronic fatigue fuifulled ICD_9 criteria for a mental disorder. McDonald, E., et al. (1993). "Chronic fatigue in general practice attenders." Psychological Medicine 23: 987-998.. Or Skapinikas et al Clarifying the relationship between unexplained chronic fatigue and psychiatric morbidity: Results from a community survey in Great Britain) Int Rev of Psychiatry 2003l 15: 57-64. conclude that "Fatigue was associated with considerable	Thank you for your comment. The committee have revised the list of differential diagnosis and added, mental health conditions: anxiety, depression or mood disorders.

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				disability, but the association between fatigue and psychiatric morbidity explained most of this disability. Unexplained chronic fatigue is a common condition, strongly associated with psychiatric morbidity." Or in Belgium, looking at the unexplained chronic fatigue pathway, "A diagnosis of unequivocal CFS was made in 23.3%. In 21.1%, CFS was associated with a sleep disorder and/or psychiatric disorder, not invalidating the diagnosis of CFS. A predominant sleep disorder was found in 9.7%, 19.0% had a psychiatric disorder and 20.8% a combination of both. Only 2.2% was diagnosed with a classical internal disease. In the total sample, a sleep disorder was found in 49.8%, especially obstructive sleep apnoea syndrome, followed by psychophysiologic insomnia and periodic limb movement disorder. A psychiatric disorder was diagnosed in 45.2%; mostly mood and anxiety disorder. DOI: 10.1016/j.jpsychores.2013.07.010 These are but a fraction of the studies that confirm that the largest single category of differential diagnoses to be considered before making a diagnosis of ME/CFS are mental disorders. 2. Previous depression is a risk factor for a subsequent diagnosis of ME/CFS. Previous depression is also a risk factor for the development of post infectious fatigue syndromes, as seen strongly after influenza and common viral infections, giardiasis and many others, including Epstein Barr virus, albeit to a lesser extent. We don't know why, but it is a clear risk factor. 3. Depression and sleep disorders are the commonest comorbidities in those with diagnoses of CFS/ME. This is partly the well-known association between depression and all long term conditions, especially those with pain and disability. But we also know this association is stronger, not weaker, in ME/CFS, as shown by a series of case control studies comparing ME/CFS with various LTCs.	

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				So for example in a Canadian population study of 115,071 randomly selected adults the conditions most strongly associated with major depression were ME/CFS (adjusted odds ratio [AOR] 7.2 [CI 5.9 to 8.8]) and fibromyalgia (AOR 3.4).” As a comparison cancer OR for MDD was 2.3 (CI 1.8 to 2.8).. Patten SB, et al, 2005, https://doi.org/10.1177%2F070674370505000402. Or in the UK among patients diagnosed with fatigue syndromes, “we found elevated baseline prevalence of: any psychiatric illness (PR 1.77; 95% CI 1.72–1.82), anxiety disorders (PR 1.92; 1.85–1.99), depression (PR 1.89; 1.83–1.96), psychotropic prescriptions (PR 1.68; 1.64–1.72) and comorbid physical illness (PR 1.28; 1.23 w1.32). DOI: 10.1017/S0033291719001065” – in the same study the prevalence ratio for depression in those with CFS/ME was 2.26 CI 2.15, 2.37) . Or in Germany, Jacob et al. 2020, 9896 cases with ME/CFS and 9896 controls without CFS [s]. Seven conditions were associated with CFS in the adjusted regression model. The disorders displaying the strongest relationship with CFS were cancer [odds ratio (OR) = 2.57, 95% confidence interval (CI) = 2.24–2.95], sleep disorders (OR = 1.88, 95% CI = 1.66–2.12) and depression (OR = 1.77, 95% CI = 1.61–1.95). doi: 10.1017/S003329172000247. 4 .This stronger link is also found when comparing with other peripheral neuromuscular disorders, part of the evidence for why the core symptoms of ME/CFS must arise from the central, not peripheral nervous system. 5 Self-reported ratings of mental health are the strongest correlations of quality of life and self-reported physical health across medicine. This is also true in ME/CFS. 6. In all long term conditions (LTCs) presence of depression is an association of poor outcome in general, and worse response	

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				to treatment – it is hard to find exceptions to this, and ME/CFS Is not one of them. So for example in the NIHR funded study of the outcomes of over 8000 patients attending specialist CFS clinics that are art of the network depression was associated with worse outcome (Collin & Crawley, BMC Health Services Research 2017: 17;488).. 7. Comorbid depression is a barrier to return to work in younger people with ME/CFS https://bmjopen.bmj.com/content/4/11/e005798 8. The links between depression and suicide are well known. In secondary care the best evidence on mortality and ME/CFS shows that only suicide is associated with a significance increase in SMR (PMID: 26873808 DOI: 10.1016/S0140-6736(15)01223-4) High quality evidence exists for all of these statements, and can be provided on request. And yet despite this, in the entire guideline depression is mentioned only once, as a signpost to the relevant NICE guidelines. The same goes for anxiety disorders and common mental disorders. Would NICE please justify this omission?	
The Royal College of Psychiatrists	Guideline	General All mentions of exercise	General	The absence in the recommendations of any mention of the benefit of exercise (0) compared to the dangers of exercise (17) is striking. But the word rest is mentioned 22 times, either neutrally or as a benefit. The number of mentions of the dangers of rest is 0. It would be preferable to discuss the pros and cons of each in a balanced and evidence based way	Thank you for your comment. After considering the stakeholder comments about the lack of clarity around what the guideline recommends on energy management and physical activity and exercise the committee made the following edits: • on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					• the section on physical activity now includes exercise • Made clear that a personalised physical activity or exercise programme includes making flexible adjustments to their physical activity (up and down as needed). This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. This guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. See evidence reviews F and G Non-pharmacological management for further information on physical activity and exercise including the committee discussion on the trade-off between benefits and harms in the evidence and the recommendations.
The Royal College of Psychiatrists	Guideline	052 - 053	031	We are concerned that the available evidence does not support this statement "The duration of symptoms before diagnosis can take place has been reduced but the criteria are now stricter, requiring that 4 different sets of symptoms are all present in order to suspect ME/CFS. The impact therefore will not necessarily be an increase in referrals but for people to receive their diagnosis earlier, which will bring forward their assessment and care plan."	Thank you for your comment. *Reduction in timeline and symptoms resolving* After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. Based on the

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				As noted above studies consistently show that around 50% of patients symptomatic with a fatigue like syndrome at 3 months post viral infection will have naturally resolved by six months. There is no data to underpin this assertion. NICE may take the view that early contact is worthwhile but they must acknowledge the potential impact on services, and also of the potential for harm from misdiagnosing a normal recovery trajectory as a ME/CFS disorder. Furthermore, the need for all four symptoms to be present before a diagnosis is made, at whatever duration, is not supported by epidemiological studies of symptoms that may follow infection (see: https://doi.org/10.1136/bmj.38933.585764.AE)	evidence and their clinical experience the committee found no reason why the time to diagnosis should be different in adults compared to children and young people noting that 5 of the 7 diagnostic criteria reviewed in Evidence review D do not have separate time referrals. As you note people with ME/CFS do experience delays in diagnosis and the committee recognised that referral to a specialist team for confirmation of diagnosis can take months, taking this into account it is important this process is started at 3 months and people are given appropriate advice until they are seen by a ME/CFS specialist team. The committee anticipate that any relevant tests would continue to exclude any other diagnoses and if symptoms resolve in the time to been seem by a ME/CFS specialist team the referral would be cancelled (please see the text below on further investigation). The committee discussed this further and considered that if there is any increase in referral by decreasing the time to refer by 1 month in adults this will be at least partly outweighed by the criteria being stricter than in the previous guideline. *Misdiagnosis of ME/CFS* The committee acknowledged and discussed the difficulty of removing a diagnosis of ME/CFS once it has been given. They edited the recommendations in the Diagnosis section of the guideline to ensure that the diagnosis is confirmed (or conversely, not confirmed) by a ME/CFS specialist team. *Further investigation/differential diagnoses.* The committee have experience of people being referred to ME/CFS specialist services and having another diagnosis and throughout the section on suspecting ME/CFS the committee have recommended that investigations should be done to exclude other diagnoses and this should continue where ME/CFS is suspected. If in any doubt specialist advice should be sought.

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					The committee have added to the criteria for suspecting ME/CFS and where 'symptoms are not explained by another condition'. *Presence of all the criteria.* The committee's discussion of how the evidence informed the recommendations is detailed briefly in the rationale and impact sections in the guideline and in more detail in the discussion of the evidence sections, here see Evidence review D-Diagnosis.
The Royal College of Psychiatrists	Guideline	004	005	None of the above is contentious. We doubt that there is any general practitioner for example who is not well aware of the importance of alternative psychiatric diagnoses in the differential diagnosis of ME/CFS. We are aware of several preventable tragedies when this has been overlooked. All of this could have been avoided if a psychiatrist had been on the committee. The absence of such a member can now be clearly seen to be a significant failing. How does NICE suggest this omission is corrected?	Thank you for your comment. The committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
The Royal College of Psychiatrists	Guideline	005	002	The College agrees with the description of how health and social care professionals should be delivering care and submits that this is exactly the approach taken by its members who are involved in the delivery of services for ME/CFS in numerous centres. Feedback data submitted as part of this consultation supports this.	Thank you for your comment.
The Royal College of Psychiatrists	Guideline	005	009	The College agrees with recommendation that an accurate and clearly delivered diagnosis is very helpful to a patient. The clinicians who responded to this consultation and who had direct experience of working in ME/CFS services would have	Thank you for your comment. The committee agree and the focus of this section of the guideline is raising awareness about the reality of ME/CFS and the impact the symptoms people with ME/CFS experience.

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				emphasised this point even more. They agreed that establishing this at the first consultation/assessment often came as a great relief to patients, who had often experienced a reluctance on the part of previous clinicians to do this, and on some occasions were reported as telling the patient that "there is no such thing as CFS/ME" They had strong opinions that ending the frustration over diagnosis, or the lack of it, was an essential prerequisite for moving forward and starting to discuss what could now be done about moving forward. We would like to see this emphasised more.	
The Royal College of Psychiatrists	Guideline	005	009	We conclude that early diagnosis is a trade-off between empowerment, illness validation and group support, contrasted with the risk of diagnosis becoming self-fulfilling prophecy of non-recovery. Unfortunately while the Committee has clearly considered the former, it has paid little or no attention to the latter and thus produced another recommendation that fails to balance benefits and risk. We suggest that this recommendation is reconsidered in the light of this balance.	Thank you for your comment. After considering the stakeholder comments the committee have replaced 'early' with 'timely' and hopes this adds clarity.
The Royal College of Psychiatrists	Guideline	007	001	The statement about needing low stimulus environment and other adaptation is not evidenced. It fails to recognise the potential harms from this advice from sensory deprivation, namely demoralisation and depression. The College recommends that a risk assessment is conducted on this recommendation owing to the potential for harm,	Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management

Consultation on draft guideline - Stakeholder comments table

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The Royal College of Psychiatrists	Guideline	008	005	A "psychological well-being assessment is usually done by a Psychological Wellbeing Practitioner. These are not GPs, physicians, psychiatrists nor psychologists, and not necessarily graduates. This recommendation continues the general theme of assigning a lower importance to mental than physical health, and further separating mind and body. We see no recommendation that the physical examination or assessment is done by a physician assistant. The mental state examination, which is not a 'well-being assessment', is as essential a part of the duty of a doctor as is the physical examination. No assessment of a chronically fatigued patient with possible ME/CFS is complete until both have been carried out as part of the same assessment. It is not something that can be left until later, cannot delegated, and we submit that no GP would ever think that they had completed their assessment and made an accurate differential diagnosis without it. How does NICE suggest this omission is corrected?	Thank you for your comment. Mental health has been included in the clinical history bullet point alongside physical health.
The Royal College of Psychiatrists	Guideline	008	010	The committee assumes that the triggering event is an infective episode, and give their opinion, that by this period of time most people will have got over the episode; in fact around a quarter are still symptomatic at this time point. NICE need to look at the evidence base for recovery rate from infections before making such a change. More importantly, the committee neglect the strong evidence that it is not just infections that trigger CFS. Any professional experienced in ME/CFS would know that major life events, major physical and psychological traumas also do, again confirmed by the literature.	Thank you for your comment. The committee doesn't assume the triggering event is an infective episode. The first recommendation in the guideline is, Be aware that ME/CFS is a ……… its pathophysiology remains under investigation'. In addition this text is in the context section, 'It is not clear what causes ME/CFS and the pathophysiology of ME/CFS remains under investigation. In many cases, symptoms are thought to have been triggered by an infection but it is not simple post-illness fatigue. It lasts longer and even minimal mental or physical activity can make symptoms worse.'

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				We suggest that this omission is corrected.	
The Royal College of Psychiatrists	Guideline	009	Box 1	We are concerned at the description of cognitive difficulties - Cognitive difficulties of "confusion and disorientation" are the hallmark features of delirium and, out with the context of pre-existing neurodegenerative illness, should be considered a medical emergency. When patients with ME/CFS say they are "confused" they are always Glasgow Coma Scale 15 and the underlying problem is often depersonalisation or derealisation. We are concerned about the potential for medical error with this advice. Whilst in practice it is unlikely this would impact on a new patient, it has considerable potential for harm in patients with known ME/CFS when undergoing urgent general medical assessment for new symptoms. The presence of true confusion or disorientation would represent clear evidence of a de novo pathological process, whereas if a doctor was influenced by NICE guideline it may be dismissed as part of the ME/CFS spectrum. We therefore additionally suggest NICE consider the legal implications of this advice with regard to malpractice.	Thank you for your comment. After considering the stakeholder comments the committee have revised the description of cognitive difficulties to, 'Cognitive difficulties (sometimes described as 'brain fog'), including problems finding words or numbers, difficulty in, slowed responsiveness, short-term memory problems, and difficulty concentrating or multitasking.' Confusion and disorientation have been removed.
The Royal College of Psychiatrists	Guideline	010	005	"*Not to use more energy than they perceive they have".* The perception of energy, which is what is being talked about, is not fixed or finite, and a wealth of research shows that it does not correlate with specific biomarkers, even when they are available, Other stakeholders are likely to comment on this, but the concept of a fixed amount of energy is scientifically misleading and in itself a message that can be iatrogenic. Likewise uncritical advocacy of rest, without any mention of the problems of excessive rest, are likely to do harm to patients, An impartial guideline would have discussed both, especially as the evidence for the side effects of prolonged rest is both voluminous and not controversial. Again, more balance is needed.	Thank you for your comment. Energy envelope After considering the stakeholder comments the committee agreed that this concept might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *Advice to rest* The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision

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					making for people with suspected ME/CFS. In reference to your comment they note there is a lack of evidence to support that advice to rest prevents deterioration and improves prognosis in people with suspected ME/CFS, but they agreed the advice would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone. The committee agreed that people should be given personalised advice about managing their symptoms and recommend this in the advice for people with suspected ME/CFS section of the guideline. * To note that after taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit Energy envelope to use energy limits.
The Royal College of Psychiatrists	Guideline	007	011	The statement that some patients are unable to digest food easily requires evidence. Otherwise this misperception risks leading to dietary modifications that risk precipitating the malnutrition and weight loss referred to under dietary management. In adolescent populations eating disorders often present with CFS like symptoms.	Thank you for your comment. The committee disagree this is a misperception, the list of the potential impacts of severe and very severe ME/CFS were identified by the committee as impacts they are aware of from their knowledge, clinical experience and are identified in the report on people with severe and very severe ME/CFS. The recommendations for people with severe and very severe ME/CFS are comprehensive and include referral to a dietician with a special interest in ME/CFS and recognise there are many reasons why a person's diet is limited. In the committee discussion in Evidence review G-non pharmacological management the committee note the importance of understanding the impact that ME/CFS symptoms can have on eating (in particular, resulting in weight loss and weight gain and that these are not necessarily the result of an

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					eating disorder) and that any assessment should be undertaken by a dietician that has this understanding to avoid a misdiagnosis.
The Royal College of Psychiatrists	Guideline	014	015 - 031	We are concerned that the recommended explanation of ME/CFS does not include the information that there is a significantly heightened risk for mental health conditions like depression and anxiety, especially in children and young people (Example Reference - Loades ME et al. The presence of co-morbid mental health problems in a cohort of adolescents with chronic fatigue syndrome. Clin Child Psychol Psychiatry. 2018 Jul;23(3):398-408. doi: 10.1177/1359104517736357. Epub 2017 Nov 2. PMID: 29096528; PMCID: PMC6150417). This will ensure that a possible change in mental health will be detected earlier, leading to better outcomes associated with early intervention.	Thank you for your comment. This recommendation does not refer to any co-existing conditions. Information on coexisting conditions is given in the suspecting ME/CFS and managing coexisting conditions sections of the guideline, and in Evidence review D- Diagnosis.
The Royal College of Psychiatrists	Guideline	016	012	No-one can be detained under the Mental Health Act simply because they have ME/CFS. Insisting that a specialist in ME/CFS be involved is like insisting that a cardiologist must be involved when someone with heart disease has to be assessed for risk to self or others. What is needed, and is a legal requirement, are medical and social work professionals trained in diagnosis, assessing the risk to the person or others, and also taking into account the views of the patient, carers or nearest relative. We believe this this recommendation has been included because there have been cases of people with ME/CFS being assessed under the Mental Health Act because of their risk to themselves, but the committee seems to misunderstand why this has happened – namely the association that exists between ME/CFS and conditions such as severe depression, which can be life threatening, fortunately a rare but not unknown situation. But no one is assessed under the MHA simply because they have ME/CFS, and no one can be detained under the MHA for that	Thank you for your comment. After considering the stakeholder comments the reference to 24 hours has been removed to acknowledge the involvement of health and social care professionals with ME/CFS may be later in the process. *Inclusion of mental health assessments in the guideline.* An assessment of mental health is included in the medical assessment in the section on suspecting ME/CFS in addition to an assessment of the impact of symptoms on psychological wellbeing. This is then repeated in the holistic assessment carried out by the ME/CFS specialist team to confirm a diagnosis and develop the care and support plan. The review section of the

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				reason. Having this statement as is in the Guidelines perpetuates the suspicion that exists in certain circles that people have been detained under the MHA "for having ME/CFS", and also perpetuates the already pervasive suspicion of psychiatry, further perpetuated by psychiatry being almost eliminated from the review. This adds to stigma and is unhelp to both patients and health professionals. An opportunity to explain what psychiatry can do and reduce myths and fears has been lost. It is another area of stark contrast to other NICE reviews of long term conditions, and most recently the draft Guidelines for Chronic Pain and for Long Covid, which approach mental health and psychiatry in an open, constructive and non-stigmatising way. Whilst this is one particular example the College is very concerned at an undercurrent of stigma towards mental disorders that appears too often in this guideline. How will NICE address this?	guideline includes an assessment of a person's condition and an assessment of their psychological wellbeing. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. No differentiation is made on physical or mental health conditions. With all assessments clinical judgment is exercised to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. This would include considering whether there are mental health concerns Also to note that after taking into consideration the stakeholder comments the committee have reviewed the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders to reflect the managing co-existing section of the guideline.
The Royal College of Psychiatrists	Guideline	022	013 - 022	"Refer people with ME/CFS to a specialist ME/CFS physiotherapy or occupational therapy service" In multi-disciplinary teams it is more usual to specify the skills required rather than be insistent on the discipline when delivering rehabilitation. Both draft NICE guidelines for Chronic Pain and the NICE guidelines for Long Covid emphasise the need for multi- disciplinary teams repeatedly – for example the draft Long Covid guidelines (8.2) state "*Provide integrated, multidisciplinary rehabilitation services, based on local needs and resources, with a range of specialist skills, including expertise in treating fatigue and respiratory symptoms, including shortness of breath. For example, a core team could comprise specialist expertise in:*	Thank you for your comment. The committee were unable to draw conclusions about the specific composition of a multidisciplinary team based on the evidence but they agreed that good care for people with ME/CFS results from access to an integrated team of health and social care professionals that are trained and experienced in the management of ME/CFS. Accordingly the committee recommended and described the expertise that should be available to a person with ME/CFS (Evidence review I _Multidisciplinary care (Benefits and Harms section). The committee recognised parts of the care and support plan should only be delivered or overseen by healthcare professionals

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				• • *occupational therapy* • • *physiotherapy* • • *clinical psychology and psychiatry* • • *rehabilitation medicine* • • *with additional expertise depending on a person's specific symptoms. "* And 5.4 *Assess people referred to integrated multidisciplinary rehabilitation services to guide management, including physical, psychological and psychiatric aspects of rehabilitation.* This is another example of serious inconsistency between Guidelines that both patients and practitioners would agree should be reasonably consistent and certainly not contradictory.	who are part of a specialist team, for example a ME/CFS specialist physiotherapist to oversee physical activity programmes. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
The Royal College of Psychiatrists	Guideline	022	014 - 022	Further to the above comment about the significant comorbidity of mental health conditions in ME/CFS, the MDT should also include health professionals trained and experienced in the assessment and management of mental health conditions and mental disorders, which may comprise, but is distinct to emotional wellbeing.	Thank you for your comment. The recommendation has been edited to include,' physical, psychological, emotional and social' to reflect that people's mental health wellbeing should be considered.
The Royal College of Psychiatrists	Guideline	022	013	Furthermore, the general tone of the guideline may have the paradoxical effect of leading to disinvestment in such teams. If no evidence based treatment can be offered to patients with ME/CFS, these resources may be better targeted at conditions that respond to rehabilitation. It is possible that such savings may be made to pay for the very considerable promised investment in services for Long Covid, which will not be accessible to the majority of ME/CFS patients.	Thank you for your comment. Throughout the guideline the importance of ME/CFS specialist services is reinforced and it is made clear where access to these services is required. The management section of the guideline sets out the interventions for supporting people with ME/CFS to manage their symptoms, including if appropriate programmes for physical activity and exercise where specialist support is needed.

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				The College is very concerned that the implementation of the guideline as stands will lead to substantive disinvestment in services for patients.	
The Royal College of Psychiatrists	Guideline	024	006	The revised document replaces the previously recommended GET and CBT with what they term 'energy management'. There is no demonstrable evidence of efficacy of 'energy management'. It looks like self-management by pacing, which the largest trial of this approach (PACE trial, 2011) showed was at best ineffective and probably worsened physical function. Can NICE please comment on this ?	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse) (see evidence review G for the committee discussion on self-management strategies). Whereas Adaptive Pacing Theory focuses on physical activity and the aim is to maximise what can be done on the one hand but to limit activity related exacerbations of symptoms on the other. With reference to the PACE trial the committee concluded that the study population was indirect and it was not clear if people had PEM, so may not reflect the population as set out by this guideline in the criteria for suspecting ME/CFS.
The Royal College of Psychiatrists	Guideline	024	021	*Uses a flexible, tailored approach so that activity is never automatically increased but is progressed during periods when*	Thank you for your comment.

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				symptoms are improved and allows for the need to pull back when symptoms are worse We agree that activity should never be "automatically" increased, and this is not a feature unique to energy management, but applies equally to both CBT and GET. CBT and GET are both collaborative treatments, and also changes are made during regular review between patient and therapist. Instead given that both energy management and CBT (and GET as well) do have a shared goal of increasing activity, this should read ""In CBT and energy management activity should be gradually increased with regular reviews that are negotiated between patient and practitioner. These may result in the need to temporarily decrease activity." Could this point be included?	After considering the stakeholder comments this bullet point has been edited to,' uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse)'. This section is about energy management and not CBT, the section on CBT includes detail on how it should be applied in managing people's symptoms.
The Royal College of Psychiatrists	Guideline	025	001	And *developing a shared understanding with the person about the main difficulties and challenges they face* • *exploring their personal meaning of symptoms and illness, and how this might relate to how they manage their symptoms* • *working together to adapt and refine self-management strategies to improve the person's functioning and quality of life, for example their 6 sleep, activity and rest* • *developing a self-management plan* • *reviewing their plan regularly to see if their self-management strategies 9 need to be adapted, for example if their symptoms or functioning change*	Thank you for your comment. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. This applies to the energy management plan. After considering the stakeholder comments recommendation 1.11.6 this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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				• *developing a therapy blueprint collaboratively with their therapist at the end of therapy.* This is a clear description of what CBT is, which we recognise and agree with. We would like to see more - a greater emphasis on engagement, which is perhaps the most important part of the assessment and early sessions, a greater emphasis on early discussions of part experiences of health care, the specifics of dealing with set-backs, how to explain this to significant others and involve them if wished, and so on.	This is an assessment for the energy management plan, a holistic assessment for the care and support plan is set out in section 1.5. and includes an assessment of previous experiences.
The Royal College of Psychiatrists	Guideline	025	025	*"Advise people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily energy levels."* Increasing activity often triggers symptoms – this is not necessarily pathological, and happens in many illnesses, convalescent periods, long term conditions, post operative surgery and so on. And it happens in exercise programmes, CBT and energy management programmes as well. It should not be unexpected, but anticipated. This advice as it stands will risk confusing excessive or prolonged symptoms, clearly to be avoided, with any symptoms, and thus risk doing harm rather than good. Ceasing or dramatically restricting all activity is associated with both physical and psychological risks, and has for many years been associated with poorer outcome, "Thus, it is suggested that interventions that either discourage avoidance of activity or enhance perceived control could benefit the course of the illness." Ray, Jeffries Weir Coping and other predictors of outcome in chronic fatigue syndrome: A 1-year follow- doi.org/10.1016/S0022-3999(97)00111-6 We suggest it is more accurate, and safer, to change this to "warn patients that they may experience an increase in	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'

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				symptoms when engaging in the right amount of activity and this may be normal and necessarily not harmful".	
The Royal College of Psychiatrists	Guideline	027	021	But we disagree with statements such as 1.11.15 (page 27, line 21) that patients should not be offered "*any therapy based on physical activity or exercise as a treatment or cure for ME/CFS* " Words like "cure" aren't the kind of language used in rehabilitation anyway, so we doubt that in practice this happens very much, but we don't see why it cannot be offered as a treatment by any standard definition of the word.	Thank you for your comment. *Treatment or cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS.
The Royal College of Psychiatrists	Guideline	027	024	There are many features of We this section with which we agree We agree that patients should only join a programme if they would like to do so (1.11.17), which is reaffirming informed consent. We agree that exercise programmes for ME/CFS should never be 'fixed' and should be tailored to the individual's needs. We agree that an programme must be personalised (1.11.20). We agree that it is necessary to stabilise activity at first (1.11.20) but disagree that this always means reduce activity, although that certainly is common We agree also that simply been told to go the gym (1.11.15) is not GET and should be discouraged. We agree with the advice against "*any programme based on fixed incremental increases in physical activity or exercise" (*1.11.16) but would point out that this is not part of the principles of GET as currently practised. And finally we agree that one needs to maintain activity or exercise at a certain level before it is time to increase (1.11.20).	Thank you for your comment. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.)

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					The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G.. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
The Royal College of Psychiatrists	Guideline	028	001	The current draft says do not offer people with ME/CFS any therapy based on physical activity or exercise as a treatment. This statement is not adequately justified. To overturn the conclusions of the WHO Guidelines that we quote elsewhere, or NICE's own guidelines on exercise and health, would normally require compelling evidence from trials that showed the opposite. No such trial exists. It would also require a convincing physiological or pathophysiological explanation of why graded exercise could go from being helpful to harmful – none has been provided, or even attempted to be provided. And finally, compelling evidence as to why a treatment or general approach known to have positive physical and psychological effects across the entire field of medicine would be different in ME/CFS.	Thank you for your comment. **After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.** *Physical activity and ME/CFS* It is commonly agreed that people with ME/CFS experience post exertional malaise (PEM) after activity. PEM is a worsening of symptoms that can follow minimal cognitive, physical, emotional or social activity, or activity that could previously be tolerated. It is

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				Can NICE please comment on this?	in this context, and recognising the evidence from people with ME/CFS indicating that misunderstanding of the impact of PEM and inappropriate advice on how to incorporate physical activity (and exercise) into their lives has resulted for some in a deterioration of their condition, that this guideline has recommended that people with ME/CFS should be supported by a physiotherapist or occupational therapist within a ME/CFS specialist team if they: • have difficulty with their reduced physical activity or mobility • feel ready to progress their physical activity beyond their current activities of daily living • would like to incorporate a physical activity programme into the management of their ME/CFS. This guideline highlights the importance of having an informed approach to physical activity and exercise in people with ME/CS that is supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS.

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					This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy 'based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS.
The Royal College of Psychiatrists	Guideline	028	001	The College accepts that there are compelling stories and narratives that people have received inappropriate advice around exercise. This seems not to be given in the context of graded exercise programmes, as recommended in the 2007 Guidelines, but more thoughtless comments from some health professionals, and/or "one size fits all" handouts, gym referrals, lack of co-produced management programmes, inadequate regular follow	Thank you for your comment. Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people

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				up or proper review. (see Gladwell et al, cited in the evidence section review). This statement requires qualification.	with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) The committee recognise that there are different definitions of the term graded exercise therapy and as a result the content and application of graded exercise therapy programmes differ. This has resulted in confusion. Graded exercise therapy is defined in this guideline as therapy based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. Graded exercise therapy consists of establishing a baseline of achievable exercise or physical activity and then making fixed incremental increases in the time spent being physically active. This definition reflects the descriptions of graded exercise therapy included in evidence review G. The committee recommended that physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories of ME/CFS, or that use fixed incremental increases in physical activity or exercise, should not be offered to people with ME/CFS. Based on the evidence mentioned above and their own experience the committee concluded that it was important that a

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					physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. **With reference to Larun 2017:** This Cochrane review looked at exercise therapy versus passive controls or other active treatments in adults with 'CFS'. The main reasons for exclusion from evidence review G are as follows: The approach to meta-analysis was different to our approach. All exercise therapies were pooled regardless of the type of exercise therapy delivered, and comparators considered 'passive' control arms (treatment as usual, relaxation or flexibility) were also pooled. We did not consider this to be appropriate for the purposes of decision-making for this guideline. Additionally, the following critical outcomes were not assessed (not primary or secondary outcomes for the review): cognitive function, activity levels, return to school/work, exercise performance measures, and mortality. However, all studies included in this Cochrane review were included in our review. We note that the Cochrane review 'Exercise therapy for chronic fatigue syndrome' (Larun et al., 2019) is contested and that it 'is still based on a research question and a set of methods from 2002, and reflects evidence from studies that applied definitions of ME/CFS from the 1990s' (https://www.cochrane.org/news/cfs) The review is currently undergoing a full update

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The Royal College of Psychiatrists	Guideline	028	008	"*Do not offer …..structured activity or exercise programmes that are based on deconditioning as the cause of ME/CFS* " This is a straw man argument. We are unaware of any programmes that are based on deconditioning as the cause of ME/CFS. This statement is inaccurate, perpetuates misunderstandings and controversy, and we would recommend it be changed. We request that it be corrected.	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise avoidance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS . Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation, 'do not offer …. physical activity or exercise programmes that are based on deconditioning and exercise avoidance theories'
The Royal College of Psychiatrists	Guideline	028	008	What however we would contend is that it is possible one consequence of ME/CFS is that patients may develop deconditioning, and that this in turn may add to their disability. If ME/CFS can lead to bed sores and the like, as the committee suggests (Guidance, page 27, line 3), it inevitably must also lead to physical deconditioning, and that trying to prevent this or ameliorate this is surely good practice, not something that should be banned. The distorted presentation of "deconditioning " is likely to prove damaging to patients. We request that it is explained properly.	Thank you for your comment. The committee have concluded that therapies based on deconditioning and exercise avoidance theories of chronic fatigue syndrome should not be offered to people with ME/CFS. These therapies assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. The committee recommended that strategies to maintain and prevent deterioration of physical functioning and mobility be included in support plans for people with ME/CFS .
The Royal College of Psychiatrists	Guideline	028	010	The College has no experience of Lightning Therapy, and it is not an approach that as far as we know is used by our members.	Thank you for your comment. *Lightning Process, osteopathy, life coaching and neurolinguisitic programming*

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				But we are troubled by the decision to reject it. It is supported by a single controlled trial (SMILE), which for once could not be downgraded on diagnostic criteria, and in which every participant reported PEM. The trial results were favourable to Lightning Therapy. We have looked briefly at the feedback and it seemed to be fairly even between positive and negative – so for example in 2.1.5.11 were found 25 negative and 18 positive sentences, and qualitative paper included both negative and positive comments. The summary in the committee's discussion seems to give greater emphasis on the undoubtedly negative comments but less to the more frequent positive comments. The College feels that this is not sufficient evidence to overturn the results of a controlled trial, and that a more reasoned response would be to suggest more evidence is needed. We use the example of Lighting Therapy, not because the College supports it, but as a mirror to the decision making process of the Committee – a single randomised trial with hopeful results, which was overturned by the committee's analysis of the qualitative data, and which led to a recommendation that the therapy be banned. We do not think that this decision was reasonable, and that the decision to drop Lightning Therapy was disproportionate to the evidence. Would NICE please comment?	After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H) The committee discussed the evidence for the Lightning Process and acknowledged that although some aspects of the therapy were found to be helpful, experiences varied. Some negative experiences were reported around the confusing nature of the educational component, the intensity of the sessions, and the secrecy surrounding the therapy. The committee were particularly concerned around the secrecy of the Lightning Process and the lack of public information on the components and implementation of the process. The committee discussed concerns that the Lightning Process encourages people to ignore their symptoms and push through them and this could potentially result in harm for people with ME/CFS. The committee noted they had made clear recommendations on the principles of energy management and this is at odds with the principles of energy management in the guideline. In addition, the committee were aware that some children had been told not to discuss the therapy with their carer or parents. The committee agreed this was an inappropriate and harmful message to give to children and young people. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and that it was appropriate to have a do not recommendation. (See evidence reviews G and H)

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The Royal College of Psychiatrists	Guideline	030	013	Although the neuropathic pain guideline is referenced there is no evidence to support a neuropathic process in ME/CFS which makes the recommendation superfluous. Yet the link to the forthcoming Chronic Pain Guidelines will pose serious problems, since the chronic pain guidelines recommend CBT and exercise. This leads to contradictory advice being given by NICE to the same population group, namely those individuals with ME/CFS and persistent pain. The committee will be aware that chronic pain is a core issue in people with ME/CFS, with a considerable number of ME/CFS patients reporting comorbid fibromyalgia, and vice versa. How does NICE intend to resolve such contradictory guidance, and what would they advise clinicians to do when faced with such a common comorbidity?	Thank you for your comment. *Neuropathic pain* The committee disagree, people with ME/CFS report many different types of pain, neuropathic pain is one of them. These are examples of NICE guidelines on pain and is not intended to be an exhaustive list of the types of pain people with ME/CFS may experience. *Chronic pain guideline* The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross refer to the Chronic pain guideline to avoid confusion. The committee note in the guideline that any when managing any symptoms or co-existing conditions in people with ME/CFS the recommendations on principles of care, access to care and energy management should be taken into account.
The Royal College of Psychiatrists	Guideline	031	015 - 017	We suggest amending 'paediatrician' to 'medical professional trained and experienced in in paediatric prescribing', to ensure that this includes child & adolescent psychiatrists who may prescribe specialist medication in collaboration with paediatricians.	Thank you for your comment. The committee agreed and paediatrician has been changed to medical professional trained and experienced in in paediatric prescribing.
The Royal College of Psychiatrists	Guideline	033	023	The guideline references enteral feeding without acknowledging the considerable harms of this process especially in the absence of neurological disorder to impair swallowing. We suggest to NICE that this could be harmful to patients.	Thank you for your comment. The committee agree that enteral feeding should take place in the context of the expertise from healthcare professionals skilled in this area. The first recommendation in this section is to refer

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					people with severe or very severe ME/CFS for a dietetic assessment by a dietitian who specialises in ME/CFS.
The Royal College of Psychiatrists	Guideline	034	005	Fatigue is a core symptom of many neurological illnesses. Meta analyses and systematic reviews confirm that fatigue is well recognised as a major problem for sufferers from MS and stroke survivors and there is strong evidence it can be helped by CBT https://pubmed.ncbi.nlm.nih.gov/31780252) , pubmed.ncbi.nlm.nih.gov/32106490. The summary for the trials of CBT versus usual care on fatigue is missing from Evidence Review G, but the nine individual trials show a consistent pattern of favouring CBT, and two already lack imprecision at the primary trial outcomes. If NICE were to decide to pool the data, we would expect a finding that CBT does improve fatigue in ME/CBT as well. There doesn't seem a logical reason why it should be different from stroke or MS anyway, given that the fatigue in ME/CFS is also of central origin (otherwise it would not be both physical and mental fatigue, in which mental and physical exertion causes post exertional physical and mental fatigue – mental fatigue being the cognitive symptoms associated with ME/CFS – concentration, short term memory, brain fog etc etc. As the committee say "even minimal mental or physical activity can make symptoms worse" (Review 71, line 28). . That being the case, CBT is a treatment for a core symptom of ME/CFS, and not just its emotional consequences, although we naturally accept that is also useful, and we would also say falls under the normal definition of treatment. Could NICE please explain why if CBT is a treatment for fatigue associated with MS and stroke, it should not be a treatment for fatigue associated with ME/CFS?	Thank you for your comment. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness. *Fatigue outcomes* Thank you for pointing out that the fatigue outcomes were missing from this section of the report; this has now been corrected. To be clear, this data was missing in error from this section of the report but was still present in other sections of the report sent out for consultation, such as in the GRADE tables and forest plots. This data was presented to the committee and was considered along with the other evidence for CBT.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

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The Royal College of Psychiatrists	Guideline	034	012	*"CBT is not curative"* "Cure" is not a concept that is used in psychological or behavioural therapies, nor in long term conditions in general. It is not even a concept that is used in much of medicine - hypertension, RA, MS, ankylosing spondylitis, Parkinson's and much else are not curable, but they are treated . However, what CBT can do is help recovery. The process of improvement. And sometimes that does seem to help some people return to how they were before they became ill. We accept this is not the commonest outcome, but even if that were to happen to only a handful, and it is in fact more than that, it would still be valuable, and that information should not be suppressed or denied. This is our evidence that people can and do recover, not often, but they do, and it is probable that CBT has played a part. Deale et al: "Predetermined criteria for "complete recovery" required that patients no longer met chronic fatigue syndrome criteria, were employed full-time, and scored less than 4 on the Fatigue Questionnaire and more than 83 on the Medical Outcomes Study Short-Form General Health Survey physical functioning scale." Seven (23%) of the CBT patients and none of the control relaxation therapy patients were deemed completely recovered (p=0.03) The authors still do not claim a cure, because one can never know if someone will still relapse in the future, but do talk about full recovery and lasting benefits for some. https://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.158.12.2038?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub++0pubmed&	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms. Curative has been included in the recommendation to reflect the qualitative evidence (see evidence reviews A) and the committee's experience that people with ME/CFS had been directed towards CBT as a cure for ME/CFS. CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness. Of the studies you reference Deale et al is included in evidence review G and Flo and Chalder, and Knoop et al were excluded as they did not meet the inclusion criteria for study design set out in the review protocol.

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				Flo and Chalder (BRAT 2014) followed 140 patients receiving CBT in routine clinical practice Six months later 37% no longer met the case definitions for CFS and 18% were fully recovered (defined as no longer meeting the criteria, their own perception of recovery and normal population levels of fatigue and physical functioning (also showed depression risk factor for poor outcomes) Knoop et al followed up 96 patients treated with CBT, again using a stringent definition of full recovery – no longer meeting the criteria, but more important the patient has to perceive his fatigue and functioning as both normal and comparable to healthy peoplel, confirmed against data from population norms. 23 % were rated as fully recovered. Psychother Psychosom 2007;76:171–176DOI: 10.1159/000099844. We also know that adolescents recover at higher rates than adults CBT is not intended to "cure" ME/CFS, any more than anti hypertensive medication "cures" high blood pressure, or drug treatments "cure" ankylosing spondylitis or rheumatoid arthritis, but can and does contribute towards recovery	
The Royal College of Psychiatrists	Guideline	034	012	A better approach to the problems of ME/CFS is not to use the language of cure, but of the potential for improvement and recovery. People can recover partially, and on occasion people do seem to return to how they were pre illness. Given that as the Committee accept we do not know what the pathophysiology of ME/CFS is, to discount that possibility seems unwise and unhelpful. There is no reason to believe that whatever illness mechanisms are identified, they will of necessity be fixed and unchanging – indeed the opposite seems more likely, although we cannot know for sure.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.

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				Perhaps the original cause of their illness, which we agree is definitely not deconditioning or abnormal illness beliefs, has resolved itself, and what remains are the consequences of illness, the normal business of rehabilitation. We do not know.	CBT is recommended where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The following recommendations set out that CBT for people with ME/CFS aims to improve quality of life, including functioning, and to reduce the distress associated with having a chronic illness.
The Royal College of Psychiatrists	Guideline	034	016	CBT *"does not assume people have 'abnormal' illness beliefs and behaviours as an underlying cause of their ME/CFS"* We agree that it does not. This is a straw man. "Abnormal illness beliefs" are not the cause of ME/CFS, any more than deconditioning is. This is not an argument that has not been advanced by researchers or practitioners in this area. CBT might be more usefully described as " a collaborative treatment in which the patient guided by the therapist tests different ways of thinking about and managing the illness with the aim of improving their health". This statement requires correction please.	Thank you for your comment. There was concern, particularly from the lay members of the committee, about the wording of CBT manuals that make suppositions about 'wrong' cognitions. The committee considered that the narrative around fear avoidance and false illness beliefs can deny patient experience, as fears can be completely rational and protective against harm. Therefore, the committee decided to specify in the recommendations that CBT does not assume people with ME/CFS have 'abnormal' illness beliefs and behaviours as an underlying cause of ME/CFS, but recognises thoughts, feelings, behaviours and physiology and how they interact with each other.(See evidence reviews G and H for the evidence and the committee discussion on these recommendations). The following recommendation includes the points about CBT being collaborative and involves working closely with their therapist.
The Royal College of Psychiatrists	Guideline	034	016	It is true is that how one thinks about one's symptoms influences outcome. This is the finding of the literature on illness perceptions. And there are plenty of studies showing how illness perceptions as measured at the start of an illness influence outcome. So for example when measured at the start of an Epstein Barr virus infection, these are associated with the	Thank you for your comment and information.

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				persistence of fatigue six month s later 10.1017/S003329171000139X ; doi:10.1017/S003329171000139X. A small trial of a psychoeducational intervention one month after the onset of EBV was acceptable to all participants and improved outcome at six months (doi: 10.1016/S0022-3999(03)00370-2)., unlike pharmacotherapy. The message here is that these are seen as perpetuating factors alongside other predictors, such as the severity of the infection. This is not unique to CFS – it relates to the experience of fatigue in other long term conditions such as MS, inflammatory bowel disease and chronic kidney disease (doi:10.1017/S0033291711000924; doi: 10.1111/apt.13870. Epub 2016 Nov 20.: https://doi.org/10.1093/ckj/sfw113. We suggest that this understanding of chronic illness is included in the review.	
The Royal College of Psychiatrists	Guideline	034	021	*is a collaborative, structured, time-limited intervention that focuses on the difficulties people are having at that time* • *involves working closely with their therapist to establish strategies that help the person to work towards meaningful goals and priorities that they have chosen themselves* • *takes into account how symptoms are individual to the person, can fluctuate in severity and may change over time*	Thank you for your comment.
The Royal College of Psychiatrists	Guideline	035	021 onwards	All of the above are basic principles of CBT, and all of the above would be common features of CBT which is used as a treatment in many other conditions, to help disability, pain, fatigue and other symptoms, not solely emotional distress. We do not think that this supports the Committee's belief that CFS/ME is a "special case", justifying what we think is a unique recommendation which ignores the evidence that as in other conditions, CBT does have an impact on primary outcomes as listed above.	Thank you for your comment. Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how

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					CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
The Royal College of Psychiatrists	Guideline	049	011	"*Based on both the evidence and their experience, the committee agreed that the Institute of Medicine's 2015 (IOM) criteria had the best balance of inclusion and exclusion of all the reviewed criteria, but it needed to be adapted for optimal use.*" The evidence review was explicit that it found no evidence to support any definition as superior compared to any other. The basis of this decision was the solely the committee's view *"based on their experience*". This statement, as it stands, has the potential to mislead the reader into believing there was underpinning scientific support for this decision. What evidence there is casts significant doubt on the specificity of IOM's criteria and their concept of Systemic Exercise Intolerance Disease, (see: https://doi.org/10.3390/diagnostics5020272), its acceptability to patients and validity (see: https://www.mp.pl/paim/issue/article/2973, https://doi.org/10.1080/21641846.2017.1362780 and https://doi.org/10.1080/21641846.2020.1757809). We suggest that NICE need to take a more balanced view toward case definitions to be consistent with the evidence.	Thank you for your comment. *Decision making in NICE guidelines* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS and with different experiences of severity. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature (as mentioned in your comment). As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed). Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the

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					clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would be no need for the committee to address this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS. The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion. The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce the number of misdiagnoses through allowing short-lived fatigue to be excluded. The committee emphasised the importance of identifying and excluding other conditions, and that these should be appropriately investigated in people with suspected ME/CFS.
The Royal College of Psychiatrists	Guideline	049	018	Again, *"Based on their experience, the committee decided that people should be given a provisional diagnosis of ME/CFS if they have all the key symptoms (debilitating fatigability, post-exertional symptom exacerbation (PESE), unrefreshing sleep and cognitive difficulties) for a minimum of 6 weeks in adults and 4 weeks in children and young people"*.	Thank you for your comment. Evidence review D-diagnosis reviews the seven diagnostic criteria for adults and two diagnostic criteria for children and young people that met the inclusion criteria set out in the protocol, these are criteria that are commonly recognised in the clinical practice of ME/CFS. It is commonly acknowledged that there is ongoing discussion in the ME/CFS community about

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				Whilst it is accepted that these four symptom groups commonly cluster in ME/CFS, the need for all 4 to be present was not supported by any evidence in the review. As noted above the evidence review was explicit that they found no evidence to support one set of criteria over another. In addition, NICE reviewers only found one study on presence of individual symptoms; it stated that PESE had sensitivity of 0.5 and specificity of 0.57. However, the committee indicated, on the basis of its own opinion, that the IOM criteria best captured the essence of ME/CFS. The underpinning evidence review in the IOM criteria (IOM 2015 https://doi.org/10.17226/19012) reported varying rates of PESE in patients with ME/CFS from 69% to 86% depending on how PESE was defined. They noted unrefreshing sleep to be present in 92% of cases, and cognitive difficulties 80% to 55% depending on definition used . It is axiomatic that the more compulsory symptoms that are listed, the more restrictive any ME/CFS definition will be but this should not be confused with being a more specific or valid phenotype. In fact, the available evidence suggests the opposite (Sullivan et al 2005 doi:10.1017/S0033291705005210). The committee found no evidence, nor did they look for any, of the rate of co-occurrence of these 4 symptoms, whether the absence of any of the four criteria always occurred in the same patients or whether in different patients. They have no data on what proportion of patients traditionally diagnosed with ME/CFS would now meet their new definition. The new definition is consequently the most restrictive definition of all those currently available. This directly contradicts the a priori decision taken in section 2.5 of the methods "For this guideline, sensitivity was considered more important than specificity" It seems difficult to justify this decision on its scientific	which diagnostic criteria should be used to diagnose ME/CFS. If there was an agreed set of criteria there would have been no need for the committee to address this question. The committee recognised this guideline adds another set of consensus criteria to the literature but noted the evidence calling for clarity over diagnostic criteria (see Evidence review B:Information and Support for health and social care professionals) and agreed that it was important to have a set of criteria that is informative and enables health and social care professionals to recognise ME/CFS. The committee made a consensus decision based on their interpretation of the evidence review comparing the criteria that the IOM 2015 criteria were a useful set of criteria, having advantages over other criteria in terms of usability and an optimum balance of inclusion/exclusion criterion. The committee note that it is the combination and interaction of the symptoms particularly with the addition of PEM, that is critical in distinguishing ME/CFS from other conditions and illness. The committee agreed that although a 6-month delay to diagnosis is built into the IOM criteria, the criteria could be safely amended by the reduction of this delay period to 3 months. It was agreed that the function of a delay is partly to reduce the number of misdiagnoses through allowing short-lived fatigue to be excluded. The committee emphasised the importance of identifying and excluding other conditions, and that these should be appropriately investigated in people with suspected ME/CFS. We note that section 2.5 of the methods manual refers to diagnostic accuracy tests and the importance of sensitivity, however the in the discussion section of Evidence review D-diagnosis there is further discussion about sensitivity and

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				basis or on the a priori decision on sensitivity made during guideline development. We suggest that NICE review this decision in the light of the evidence.	specificity in the context of the development of criteria, noting that here specificity is important. This section also includes a discussion on the heterogeneity in the study populations.
The Royal College of Psychiatrists	Guideline	050	005	*"The committee discussed the non-specific nature and common presentation of some ME/CFS symptoms (for example, cognitive difficulties such as brain fog), Because of this, the committee agreed it is important that when a healthcare professional suspects ME/CFS, they should also consider alternative explanatory diagnoses or coexisting conditions".* We note that the committee were therefore cognisant that the symptoms of ME/CFS were non-specific, and agreed that a health care professional should consider alternative diagnoses. Unfortunately, these did not include the commonest alternatives to be considered in the differential diagnosis of ME/CFS, namely psychiatric diagnoses, a major oversight that reflects the lack of general mental health expertise in the committee. We suggest that this omission requires correction.	Thank you for your comment. The committee have revised the list of differential diagnosis in evidence review D and added, mental health conditions: anxiety, depression or mood disorders.
The Royal College of Psychiatrists	Guideline	051	022	We are concerned at the potential for over diagnosis following this decision- "The committee agreed that although a 6-month delay before diagnosis is built into the Institute of Medicine criteria, the criteria could be safely amended by reducing this period to 3 months" No evidence was used to support this decision, just a committee view that symptoms from acute infection would have resolved by then. By contrast epidemiological survey data appear to show a consistent picture eg Hickie et 2006 that approximately 27% of patients following EBV, Q fever or Ross River virus will have symptoms akin to ME/CFS at 3 months but this falls to 12% by 6 months. Most if not all studies of corroborated post-infectious fatigue syndrome find similar reduction in prevalence over the first six months	Thank you for your comment. After clarifying that ME/CFS is suspected at 4 and 6 weeks and this is not a provisional diagnosis the only reduction in the time to diagnose ME/CFS from the previous NICE guideline on CFS/ME is now in adults and it is reduced by 1 month. See evidence review D-diagnosis for the evidence and committee discussion on the diagnostic criteria.

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				(studies reviewed in the COFFI collaboration. See: https://doi.org/10.1080/21641846.2018.1426086	
The Royal College of Psychiatrists	Guideline	057	023	"*The quantitative and qualitative evidence was mixed, and this reflected the committee's experience. Based on criticisms in the qualitative evidence of CBT being used as a 'treatment' for ME/CFS, the committee considered it was important to highlight that CBT is not a cure for ME/CFS and should not be offered as such, but that it is a type of supportive psychological therapy which aims to improve wellbeing and quality of life and may be useful in supporting people who live with ME/CFS to manage their symptoms. It should therefore only be offered in this context*. Once again we emphasise that as far as we are aware in the services in which our members work, CBT is not offered as a "cure", and that this would be counter to the general use of psychological and rehabilitative therapies across the NHS. "Cure" is simply not a word that enters the lexicon, and that this is setting up a "straw man" and not very helpful since it's not in common usage. In our experience we struggle to remember patients who have asked "is CBT a cure?", they are much more likely to say "Can CBT help me?" We suggest this should instead read: "CBT is offered to help support patients, and can also help the journey towards recovery", both statements being accurate.	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
The Royal College of Psychiatrists	Guideline	071	011	*"There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic"* Could the panel explain why they think this is problematic? And if so, why was a change made to the previous convention of calling this condition "CFS/ME"?	Thank you for your comment. The committee agrees there is controversy over the terms used to describe ME/CFS and this is reflected in the stakeholder comments. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was initially set out in the scope for the guideline, *'This guideline*

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					scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names' and then readdressed in the context section of the guideline, *'The terms ME, CFS, CFS/ME and ME/CFS have all been used for this condition and are not clearly defined. There is little pathological evidence of brain inflammation, which makes the term 'myalgic encephalomyelitis' problematic. Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental. For consistency, the abbreviation ME/CFS is used in this guideline.'*
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D			And central to this is the issue of post exertional malaise (PEM) or PESE as the Committee now describes it. What they say is that this is key symptom in ME/CFS and because neither Oxford nor Fukuda mandate the presence of this one symptom – the one says it should be recorded the other that is a diagnostic criteria, but do not make it mandatory, both criteria are fundamentally unsound . The committee discuss this at length in three places.	Thank you for your comment. The four symptoms (debilitating fatigue, PEM, unrefreshing sleep and cognitive difficulties) were agreed by the committee as the best basis for identifying people with ME/CFS and as essential to a diagnosis of ME/CFS. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). This point we think refers to the decision by the committee to downgrade evidence that did not use a diagnostic criteria that includes post exertional malaise (PEM) as essential. PEM is widely acknowledged in ME/CFS specialist practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just do not know how many if the information is not reported.

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					Where this is the case, the trial population could include people that do not have ME/CFS and this makes it difficult for the committee to be confident of the benefits and risks of the interventions on people with ME/CFS. Using GRADE and CERQual the committee agreed that evidence without this information would be 'indirect' (relevance in CERQual) acknowledging this uncertainty about the population. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and CERQual. After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the quantitative and qualitative evidence and the application of indirectness and relevance. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods	006	025	WE cannot understand the decision making outlined in 'Table 2 Review Questions Chapter Identification and diagnosis' "In people with suspected ME/CFS, what are the criteria used to establish a diagnosis?....Outcome- Published criteria" It seems bizarre that no attempt has been made to answer the question that is of central importance to most clinicians- how often is ME/CFS misdiagnosed and does that rate alter depending on what criteria are used. (See comments from NHS England and RCGP, who prioritise this question, in the consultation period).	Thank you for your comment. The areas of the scope are agreed before the development of the guideline starts. All NICE guidelines follow the process for evidence reviews as set out in Developing NICE guidelines: the manual. This guideline was no exception. The review protocol is developed by the review team and the guideline committee. The review protocols were drafted by the reviewing team and then refined and agreed with the committee members. It is then reviewed and approved by NICE staff with responsibility for quality assurance. The input of the committee is

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				The diagnostic accuracy of individual symptoms and signs is explored, albeit in an idiosyncratic fashion, but the value of the global assessment and added value of utilisation of different diagnostic criteria is not. Given the paucity of disorders in which individual signs are pathognomic, missing the opportunity to assess a criteria driven approach to diagnosis seems an obvious failing.	critical in ensuring that the protocol will identify the evidence that is relevant to answer the question informing clinical practice.
The Royal College of Psychiatrists	Methods	006	025	We cannot understand the decision making in Table 2 "Review Questions Chapter Identification and diagnosis What is the diagnostic accuracy of specific tests, or clinical symptoms/signs to identify ME/CFS in people with suspected ME/CFS? Outcomes - Diagnostic RCT"- In a condition such as ME/CFS where highly effective treatments are not available diagnostic RCT data seems unlikely. Further, it seems bizarre to designate mortality outcomes as critical rather than important. This is particularly the case when the largest studies show no increase in SMR. See https://doi.org/10.1017/S0033291719001065 and http://dx.doi.org/10.1016/S0140-6736(15)01223-4 The average age of onset of ME/CFS is 33 which, with weighting for sedentary life, equates with an average life expectancy of a further 50.3 years. This would effectively mean that the value of CT imaging, for instance, could not be considered as it has only been available for 44 years. Finally, 13 variables are judged critical and it is highly unlikely any RCT would encompass them. We were left wondering what the committee hoped to achieve in setting such an improbably high bar- were they seeking evidence or seeking to discount evidence.	Thank you for your comment. All NICE guidelines follow the process for evidence reviews as set out in Developing NICE guidelines: the manual. This guideline was no exception. The review protocol is developed by the review team and the guideline committee. The review protocols were drafted by the reviewing team and then refined and agreed with the committee members. It is then reviewed and approved by NICE staff with responsibility for quality assurance. The input of the committee is critical in ensuring that the protocol will identify the evidence that is relevant to answer the question informing clinical practice. In any systematic review informing a guideline it is important to include outcomes that are important to clinical practice and the people with the condition (The COMET initiative provides some useful background on this https://www.comet-initiative.org/) When developing the protocols for the evidence reviews the committee agreed that mortality was an important outcome to measure when evaluating interventions. This is a standard measure to include when assessing the clinical and cost effectiveness of an intervention.
The Royal College of Psychiatrists	Methods	006	025	We cannot understand the rational of timepoint selection behind the choice of "Table 2 Diagnostic RCT CRITICAL (reported at longest follow up available)": It is standard statistical practice to set a primary endpoint in a study that should be used for	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline

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				analysis. It can be the case that longer term outcomes are reported but these are almost always exploratory endpoints for future hypothesis generation taken after patients have left the confines of a trial and usually with considerable loss to follow up. Standard trials practice, regarding such data, are that the outcomes at end of treatment and most importantly primary endpoint also need to be given. This decision deviates so far from standard guideline methodology that it needs *evidence-based* justification. Again, we were left wondering whether the committee were they seeking evidence or seeking to discount evidence.	was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Methods	009	Management of ME/CFS	"*What is the clinical, cost-effectiveness and acceptability (including patient experiences) of non-pharmacological interventions for people with ME/CFS?"* Again, the methods described this clear aim, which is "for people with ME/CFS", not people with ME/CFS who have endorsed PEM on a questionnaire, which the evidence shows is not particularly robust. Since this symptom is very common but not pathognomonic for ME/CFS, the later reviews deviate from this aim, but excluding trials that do not mandate PEM, and only providing guidance for those with ME/CFS who also have PEM. Could NICE comment please?	Thank you for your comment. The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience

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					PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence. When considering the stakeholder comments about the inclusion of PEM in the diagnostic criteria of ME/CFS being applied differently across the evidence reviews, the committee agreed the requirement of PEM was particularly important in the studies evaluating interventions. The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. Whereas in the evidence reviews exploring the experience of people about services and information and support needs the presence of PEM is less likely to have an impact on the findings.
The Royal College of Psychiatrists	Methods	009	Table 2	The methods section shows that all outcome data should be reported at longest follow up available. This is an unusual and problematic instruction. Some reviews don't do this, - the Chronic Pain didn't. Others such as chronic low back pain, another long term condition, used	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set

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				greater or less than four months. An analgesic review used 2 and 6 weeks, but did use "longest time reported" for mortality and GI side effects, which makes sense. Irritable bowel syndrome review used longest available follow up, but also presented other time points as well. Depression in adults with a chronic physical health problem, another overlapping review, looked at the impact of physical activity the end of treatment. We haven't looked in any depth, but as far as we can see, "longest available follow up" was not used as the sole measure in any review in a similar area. Why was this chosen as the sole outcome measure for the ME/CFS review?	out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.
The Royal College of Psychiatrists	Methods	009	Table 2	The most obvious consequence of this decision is that it directly led to inappropriate and misleading conclusions in what could hardly be a more important measure – outcome data. Modern ethics committees often insistent at that some point during the life of a trial patients will for ethical reasons need to be offered one of the other treatments in the trial that they were not allocated at randomisation. The most obvious example is when the Data Monitoring Committee (DMC) decides that the trial question has now been answered and it is unethical to allow the participants to remain in their allocated group. In the White et al (2011) trial, which did have a Data Monitoring Committee that did not happen during the duration of the trial. But the ethical approval for the trial did stipulate that after the end	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and

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				of the trial, participants should be offered any of the treatments that had been tested in the trial, should they so choose. Again, this is merely good practice, and patients have often sought the active treatment once they have come to the end of the trial. Meanwhile, the triallists obtained the resource for a further follow up, which happened 135 weeks after randomisation. Again, this is not unusual, such longer term endpoints can be important for understanding late outcomes within groups but this should not be confused with assessment of efficacy between groups. This is particularly clear when the original group allocation had now ended. Making direct comparisons between groups no longer makes much sense. This is what happened in this Review. Even worse is the fact that by not having any other outcome data points, this was obscured. In particular, the most important data point, the protocol stipulated and monitored trial end point of 52 weeks, was lost for both primary outcomes, and replaced by the misleading 'longest available data'. Might NICE indicate how this will be corrected please?	not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. GET is described as in the PACE trial as based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. A successful intervention addressing avoidance of activity should have long term evidence of efficacy as defined by the outcomes in the study protocol, assuming the aim is for avoidance of activity to be reversed.
The Royal College of Psychiatrists	Methods	009	Table 2	The second inevitable consequence is an obvious one – the longer the follow up, the greater the loss to follow up. White et al (2011) had what everyone will accept was a remarkable follow up for a non-pharmacological, or indeed any trial, at one year outcome - 95% of those randomised, with no differential loss to follow up, and no contamination or cross over. But, of course, at 135 weeks there was indeed cross over/contamination, which was deliberate, and the numbers had diminished. The inevitable result of both to render meaningless the between group comparison that was made in the Review, and to also be able to make a rating of "imprecision", which was not true at the 52 week primary end point.	Thank you for your comment. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available.

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				The same would have happened to the Deale et al trial of CBT, which actually had managed a reasonable five year follow up. But because the primary endpoints could not be extracted at five years, there was no choice but to report the 6 month primary predetermined end point. What was reported was the long term impact on employment (a sensible measure to asses with the longest available data) which was significant, but not the data at five year showing that CBT remained superior to usual care/ relaxation and had reduced relapses during that time. So there will still be inconsistencies, but at least the primary end points of the trial were reported. Why was this not done also for the White et al (2011) trial – the largest trial of rehabilitative interventions in this field? Might NICE indicate how this will be corrected?	Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. GET is described as in the PACE trial as based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. A successful intervention addressing avoidance of activity should have long term evidence of efficacy as defined by the outcomes in the study protocol, assuming the aim is for avoidance of activity to be reversed.
The Royal College of Psychiatrists	Methods	009	Table 2	Prioritising longest follow up data available obscures more relevant data, most importantly the results of the trial at the pre-set end points. It also creates a systematic trend towards greater imprecision, for the simple reason that numbers reduce. As very little in the way of data pooling was done, this would not be corrected. This will normally have been considered in the Methods Review, yet there is no mention there of precision around time points. So normal practice would be that if you have a point estimate for an outcome that shows benefit, but the CIs cross one, you would refer to earlier time points for that outcome to see if the effect was a) demonstrated; and b) the confidence intervals showed that you are fairly certain of an effect. This would lead you to have more confidence in your point estimate for the later time point, and you may well not downgrade for imprecision, and make a note to this effect. But if you have ensured that the highly informative evidence taken before that last outcome, you have clearly introduced a systematic bias against trials with longer	Thank you for your comment. All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. Reviews are underpinned by protocols, these are developed and agreed by the guideline committee and set out the approach for the evidence synthesis before the data is collected. There is no standard approach to choosing timepoints for NICE reviews as this depends what each committee considers useful for decision making for the particular condition or intervention being assessed. Data was extracted at the longest follow-up available, as specified in the protocol for this review. There is an increasing call for evidence to reflect the real-world situation of patients and not just that of ideal and controlled short term circumstances. The committee considered that long-term data of treatments for ME/CFS to be more reflective of real-world efficacy and more

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				follow up, which makes little sense. Such data would normally be used to draw conclusions such as "The benefits of Treatment A were clear 12 months after the start of treatment, but in the trials with longer follow ups did not persist at three or five years", provided of course that you were confident that the original random allocation was still valid at that time. For many of the therapies considered in this report the normal practice would be to suggest "booster" sessions for example, which is what happens in some ME/CFS services already. Does NICE agree that insisting on "longest available follow up" had the unintended consequence of giving a misleading and false impression of the outcomes of the largest trial of both CBT and GET ever undertaken, and significantly distorted the conclusions of the evidence synthesis available to the reader and the Committee?	helpful for decision making and implementation in clinical practice. Longer term follow-up reflects the likelihood that people may decide to discontinue the treatment and change treatments, this is an important consideration when making recommendations for interventions. As such, we did not extract the shorter timepoints where longer follow-up was available. GET is described as in the PACE trial as based on the deconditioning and exercise avoidance theories of ME/CFS. These theories assume that ME/CFS is perpetuated by reversible physiological changes of deconditioning and avoidance of activity. These changes result in the deconditioning being maintained and an increased perception of effort, leading to further inactivity. A successful intervention addressing avoidance of activity should have long term evidence of efficacy as defined by the outcomes in the study protocol, assuming the aim is for avoidance of activity to be reversed. Of note are the drop rates in the PACE trial and further exploration of this would support future decision making in updates of the guideline. *Imprecision* NICE uses GRADE to evaluate the quality of the evidence, this includes the assessment of imprecision. The application of imprecision is describes in section 2.6.1.4 of the methods report. The assessment was the standard approach used in NICE guidelines. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of

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					stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
The Royal College of Psychiatrists	Methods	009	Table 2	Had there been no policy of only using "longest available follow up" then the White et al trial would almost certainly have not been down-graded for imprecision, since we can see that for the other less important secondary outcomes that were not collected 135 weeks but only at the 52 week endpoint Does NICE agree?	Thank you for your comment. The imprecision rating for the outcomes at 52 weeks has not been calculated as the data has not been extracted, as a result it is not possible to say *if the outcomes in* White et al trial would almost certainly have not been down-graded for imprecision.
The Royal College of Psychiatrists	Methods	009	Table 2	But imprecision was an issue for many of the smaller trials. The normal way of looking at this is to carry out data pooling, followed by sensitivity analyses, tests for heterogeneity and so on. But these were not done. The College cannot see any explanation, discussion or acknowledgement of this inbuilt systematic bias towards greater imprecision, magnified by the relative lack of data pooling.	Thank you for your comment. All NICE guidelines follow the process for evidence reviews as set out in Developing NICE guidelines: the manual. This guideline was no exception. The review protocol is developed by the review team and the guideline committee. The review protocols were drafted by the reviewing team and then refined and agreed with the committee

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				Can NICE explain why this is?	members. It is then reviewed and approved by NICE staff with responsibility for quality assurance. The input of the committee is critical in ensuring that the protocol will identify the evidence that is relevant to answer the question informing clinical practice. *Data pooling* The protocol sets out what data is to be combined, this includes the types of interventions and the outcomes. Interventions are combined where clinically this is plausible, where they are the same or very similar intervention. Outcomes are combined where they measure the same outcome and the scales used are able to be combined. Where there is heterogeneity (as set out in the methods chapter) sensitivity analysis is undertaken. The reviewing team check with the committee that they have combined or not combined the interventions appropriately.
The Royal College of Psychiatrists	Methods	012	008	There is also an inconsistency within the Review. The review set a threshold *"Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group."* Any threshold is ultimately arbitrary and this choice has been applied inconsistently. The Cochrane Collaboration set a similar threshold for their reviews on treatment in ME/CFS but now have been discounted by NICE as being too heterogeneous on this basis.	Thank you for your comment. *Stratification* This refers to the threshold for: • Age; children, young people and adults (under 12 years, 12-18 years and over 18 years) • Severity of presenting symptoms: severe vs not severe as defined by the studies Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group. This has not been applied inconsistently or the reason the Cochrane reviews were not included. The committee make a judgment about when they consider that a population in a study will reflect the population in the protocol. They take into account how the heterogeneity in a population will impact on the results. For example, if a study includes 20% of children under 12 years, it would not be considered as

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					representative of children under 12 years . The intervention may not reflect the impact on children under 12 years. This is important when considering the evidence for guidelines. In this guideline children and young people were identified as a group for special consideration and the data stratified accordingly to enable the committee to have the most appropriate evidence to support their decision making.
The Royal College of Psychiatrists	Methods	012	008	We are concerned by an inconsistent approach to the handling of evidence. The review set a threshold *"Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group."* This is a very arbitrary cut off. If you are conducting a single trial, then you define these cut offs precisely at whatever level or for whatever reason. But when you are conducting a systematic review of randomised controlled trials, then you should avoid being restrictive with your inclusion criteria in this kind of way to avoid the accusation of developing criteria that are intentionally restrictive and which then exclude trials that might be informative, and which may have used a variety of different thresholds. So normal practice would be to make the inclusion criteria as inclusive as possible, excluding studies that were obviously irrelevant, which would not mean that they had for example 89% of cases within the threshold. And then you conduct a sensitivity analysis against the criteria if you really believe it is going to be a substantive effect modifier. Might NICE indicate how this will be corrected please?	Thank you for your comment. *Stratification* This refers to the threshold for: • Age; children, young people and adults (under 12 years, 12-18 years and over 18 years) • Severity of presenting symptoms: severe vs not severe as defined by the studies Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group. This has not been applied inconsistently or the reason the Cochrane reviews were not included. The committee make a judgment about when they consider that a population in a study will reflect the population in the protocol. They take into account how the heterogeneity in a population will impact on the results. For example, if a study includes 20% of children under 12 years, it would not be considered as representative of children under 12 years . The intervention may not reflect the impact on children under 12 years. This is important when considering the evidence for guidelines. In this guideline children and young people were identified as a group for special consideration and the data stratified accordingly to enable the committee to have the most appropriate evidence to support their decision making.

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The Royal College of Psychiatrists	Methods	012	008	We are concerned by an inconsistent approach to the handling of evidence. The review appropriately set a threshold "Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group." But then this threshold is subsequently inconsistently applied throughout the guideline. For example, Cochrane Collaboration set a similar threshold for their reviews on treatment in ME/Chronic Fatigue but were discounted by NICE as being too heterogenous for this decision that actually aligns with NICE's prespecified thresholds. Can NICE explain what this inconsistent approach has been applied?	Thank you for your comment. *Stratification* This refers to the threshold for: • Age; children, young people and adults (under 12 years, 12-18 years and over 18 years) • Severity of presenting symptoms: severe vs not severe as defined by the studies Where studies reported a mix of populations across strata, a threshold of 90% was agreed with the committee as a cut off for what would be acceptable to constitute a predominant group. This has not been applied inconsistently or the reason the Cochrane reviews were not included. The committee make a judgment about when they consider that a population in a study will reflect the population in the protocol. They take into account how the heterogeneity in a population will impact on the results. For example, if a study includes 20% of children under 12 years, it would not be considered as representative of children under 12 years . The intervention may not reflect the impact on children under 12 years. This is important when considering the evidence for guidelines. In this guideline children and young people were identified as a group for special consideration and the data stratified accordingly to enable the committee to have the most appropriate evidence to support their decision making.
The Royal College of Psychiatrists	Methods	015	024 - 026	*"For intervention reviews, randomised controlled trials (RCTs) were included where identified as because they are considered the most robust type of study design that can produce an unbiased estimate of the intervention effects."* So why did the committee prioritise qualitative study and patient group survey findings on the safety of graded exercise therapy over the RCT evidence of safety? Two large trials of GET or a guided self-help approach, based on GET, showed six different	Thank you for your comment. Developing NICE guidelines: the manual. Chapter 4 *Developing review questions and planning the evidence review* addresses the topic about approaches to take when considering the design of studies to be included in a systematic review. In summary the effectiveness of an intervention is usually best answered by a RCT because a well-conducted RCT is most likely to give an unbiased estimate of effects. When developing

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				safety outcomes were no more frequently reported after GET than comparison interventions (White et al, 2011, https://doi.org/10.1016/S0140-6736(11)60096-2; Clark et al, 2017, http://dx.doi.org/10.1016/S0140-6736(16)32589-2) Could NICE comment please?	the protocols for the intervention reviews, a RCT was agreed to be the most appropriate study design to evaluate clinical effectiveness. The committee agreed there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. In recognition that the views of people with ME/CFS who had experienced the interventions was important a qualitative review was done with an accompanying call for evidence to identify any unpublished evidence. People with ME/CFS reported harms in the qualitative evidence. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
The Royal College of Psychiatrists	Methods	017	044	We are concerned about the inconsistent application of this statement with regard to the diagnostic value of individual clinical symptoms and signs "For this guideline, sensitivity was considered more important than specificity on the basis that at an early point in the diagnostic process, it is of greater importance to avoid false negative results and excluding people from a diagnosis". The statement itself is reasonable but it is not applied uniformly across the guideline. For example, the vast majority of randomised trials in the literature are excluded despite having used internationally recognised diagnostic criteria on the sole grounds that they did not agree with a new criteria that NICE	Thank you for your comment. No study was excluded because recruitment did not include PEM as an essential criterion. *PEM* The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do

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				committee simply made up absent any supporting evidence based solely on their internal committee deliberations that their newly made up definition might better capture the essence of ME/CFS than criteria which have been subject to widespread international usage. We request NICE cite a single comparable example from comparable guideline on any topic or by reference to a highly cited methodology paper that supports such a strategy.	not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods	019	005	The College is concerned that the Committee has failed to use the GRADE system appropriately and has consequently introduced double jeopardy into its decision making processes. The committee indicate in numerous places that they regarded non blinded trials with self-reported outcomes as worthless. This view was backed up by Professor Edwards in his expert testimony where he described such trials as "uninterpretable". However, the GRADE system that was being used in the work of	Thank you for your comment. GRADE has been applied using the same approach as NICE guidelines as this is reflected in the methods chapter. The reference to evidence review G reflects the committee's discussion. The acknowledgement of the lack of existing objective outcome measures of effectiveness of interventions for

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				the evidence group already accounted for this in the ratings of the evidence team as outlined in the methods section: *"Risk of bias; Risk of bias were evaluated using the Risk of Bias checklist. The main domains of bias for RCTs are listed in Table 5. Each outcome had its risk of bias assessed within each study first. For each study, if there were no risks of bias in any domain, the risk of bias was given a rating of 0. If there was risk of bias in just domain, the risk of bias was given a 'serious' rating of −1, but if there was risk of bias in 2 or more domains the risk of bias was given a 'very serious' rating of −2. An overall rating is calculated across all studies by taking into account the weighting of studies according to study precision. For example, if the most precise studies tended to each have a score of −1 for that outcome, the overall score for that outcome would tend towards −1."* The accompanying Table 5 makes it clear that performance bias is included in the list of biases that the Review Team assessed. This was appropriately dealt with by deciding that only outcomes that used validated questionnaires were to be included. In other words, the problem was noted by the NICE Methods group and an appropriate solution, based on validated questionnaires, was scored within the GRADE system to cover performance bias. This was in keeping with all other NICE Guidelines. However the Committee then make what appears to be an error of further reducing their confidence in the results for exactly the same reason: "*3.2.1 Summary of quality for review of clinical and cost effectiveness* *"The majority of the evidence was of low and very low quality. The main reasons for downgrading were risk of bias, indirectness and imprecision. There was a lack of blinding in the studies due*	ME/CFS and the limitations of subjective measures is as you note reflected in the GRADE rating. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).

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				to the nature of the interventions. This, combined with the mostly subjective outcomes, resulted in a high risk of performance bias. The committee considered this an important limitation when interpreting the evidence." Or as repeatedly stated "*The committee acknowledged the lack of existing objective outcome measures of effectiveness of interventions for ME/CFS and the limitations of subjective measures (see Professor Edwards expert testimony – Appendix 3: Expert testimonies).*" *(ex Evidence Review G, 316, 29: Evidence Review J, 9; 32 ; Evidence Review E 13. 28; Evidence Review D 64;18*). On the face of it, it seems that Professor Edwards' testimony has misled the committee, with the result that a persistent bias existed against all trials which used unblinded interventions and self-reported measures, even if assessed by validated questionnaires, in addition to the ratings assigned by the Grade system. If NICE feels that the committee was unduly influenced by what they heard, how can this be resolved?	
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. page 313, Review D, Section 1.2.5.1 D:		We can find no evidence that the Review attempted to find any evidence to support their supposition or opinion, but instead told the team carrying out the reviews of the evidence to impose a rating a "serious risk of indirectness" on every trial that used these criteria. Does NICE agree?	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.

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					PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	Population indirectness was undoubtedly considered very important. The discussion centres largely on the CDC 1994 ("Fukuda") criteria, which are far and away the most cited criteria in CFS research, with over 3800 Scopus and 5700 Google scholar. It remains the most used criteria to this day, with 160 citations annually used by all disciplines including the biomedical, and is the most often recommended criteria in 27 European countries again to this day. The second is the Oxford criteria, with 750 citations, still being used about 25 times a year, and the third is the 1988 Holmes criteria, now rarely used. No other criteria comes close. The committee discuss this in at least three places and give their opinion that these criteria are not	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.

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				appropriate for research, because using these criteria could end up including people in studies that would create a selection bias, because people would be included who do not have ME/CFS, but instead have some other condition that might response better to CBT or GET, and would therefore falsely give a favourable impression of these treatments.	PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	First,: Methods Review, 20, line 8 "*In this guideline population indirectness was important to take consider. The committee considered the diagnostic criteria used in the studies to recruit eligible participants. The committee agreed that some diagnostic criteria that have been used in the past may not accurately identify an ME/CFS population and it is likely that the use of such criteria has resulted in people misdiagnosed as having ME/CFS being included in the studies. Post exertional symptom exacerbation was identified as central to the diagnosis of ME/CFS and the committee noted that some criteria have not included this as a compulsory requirement. The*	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.

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				inclusion of non-cases may have obscured the true effect of the different interventions on people with ME/CFS and this raised concerns over the generalisability of findings to the wider ME/CFS population. The committee agreed to downgrade evidence for population indirectness where studies used diagnostic criteria for entry that do not include Post Exertional Symptom Exacerbation as an essential symptom. This included the CDC 1994 criteria, upon which the majority of the evidence was based, as well as the CDC 1988 and Oxford criteria" Section 3.2.1. Evidence review G "*The committee agreed that a population diagnosed with such criteria may not accurately represent the ME/CFS population and that people experiencing PEM/PESE are likely to respond differently to treatment than those who do not experience PEM/PESE and this raised concerns over the generalisability of findings to the ME/CFS population. It was therefore agreed to downgrade the evidence for population indirectness.* *Evidence was not stratified by diagnostic criteria used, so theoretically, studies including potentially different populations could have been combined*". Section 1.2.5.1 Evidence Review D: *If interventions are based on evidence that include other populations (for example using the broader criteria) this could result in the implementation of interventions that are potentially ineffective for subsamples of patients. The committee noted that the majority of the studies conducted in this area have recruited participants using criteria that do not include post exertional malaise/post-exertional symptom exacerbation as key inclusion criterion and include broader interpretations of fatigue alongside PEM/PESE. Arguably this has resulted in heterogeneous study*	PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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				populations with subsamples of people with different conditions. It is difficult to know the number of people that have PEM/PESE and are considered in the tighter criteria to have ME/CFS. The committee agreed this proposed some difficulties in interpreting evidence that did not include PEM/PESE as a key diagnostic criterion with the potential of an overestimation or underestimation of association or effect. As a result the committee agreed to consider the evidence based on inclusion criteria that did not include PESE as a compulsory feature for diagnosis as 'indirect', on the basis that it was difficult to be sure if the population consisted only of people with ME/CFS. Question: Does NICE agree that at no time do the committee express a firm view on this, it is caveated by may" (3), "likely" (2) ," could" (2), "raised concerns", "theoretically", "potentially", " arguably"," "potential" , and "difficult to be sure" "	
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	For example, it would be normal practice to carry out a sensitivity analysis to compare if the few trials of non-pharmacological interventions that did use criteria that mandated PEM found a differing picture to the trials that did not. There were only two trials that used definitions mandating the presence of PEM. The first was GETSET for graded exercise, and the second was the SMILE trial, the only trial of the Lightning Process. We can find no evidence that such a sensitivity analysis was carried out. This would normally be standard practice. The consequences of not doing so would be profound. Otherwise the Committee are saying that 90% of those who participated in the clinical trials were deemed to have a "serious risk" of not having ME/CFS, even though the participants self reported that they did, and the clinicians and staff who assessed them reported that they did. Exactly the same would apply to all of those who took part in the qualitative studies, since as we shall see, very few of those would have not been rated as also as "serious risk" of not having ME/CFS.	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported.

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The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	We have been able to obtain more data that was not available to the committee, unlike the GETSET and PACE trials, by asking the PIs of as many as we could locate in the time available if they had recorded PEM data in their study. We considered it likely that they had, since it is a criterion in the CDC 1994 definitions. This is what we have obtained. We expect that given time and also the lifting of the COVID restrictions on return to work more is out there. But the data is clear. Does NICE consider that this is sufficient evidence to revise the ratings of indirectness, as all report that the vast majority of those in trials that were rated as indirect on the basis of non-mandatory reporting did in fact endorse the PEM criterion. There is no reason to believe, and every reason to expect, that the situation is the same in the outstanding trials?	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported. The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported.

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<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>Study</td><td>% of patients reporting PEM</td><td>Fatigu sever</td></tr>
<tr><td>Prins et al, 2001</td><td>275/278 (99%)</td><td>+*</td></tr>
<tr><td>Stulemeijer et al, 2005</td><td>68/71 (96%)</td><td>+</td></tr>
<tr><td>Moss Morriss et al 2005</td><td>48/49 (98%)</td><td>?</td></tr>
<tr><td>Wearden et al 2010 (FINE)</td><td>293/296 (99%)</td><td>?</td></tr>
<tr><td>Knoop et al, 2008</td><td>163/169 (98%)</td><td>+</td></tr>
<tr><td>Nijhof et al, 2012</td><td>117/135 (87%</td><td>+</td></tr>
<tr><td>Tummers et al, 2012</td><td>119/123 (97%)</td><td>+</td></tr>
<tr><td>Wiborg et al, 2015</td><td>179/204 (97%)</td><td>+</td></tr>
<tr><td>Janse et al, 2018</td><td>231/240 (96%)</td><td>+</td></tr>
</table>
</td><td>To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness.

*After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

To note. We looked for any published information on the percentage of participants with PEM in the included trials, or subgroup analyses in study participants with PEM. The papers for all included studies were reviewed again, as well as any published supplements. The excluded studies list was also re-examined to ensure any relevant information relating to PEM in the included studies were not missed. Unpublished data was not accepted for this analysis.</td></tr>
<tr><td>The Royal College of Psychiatrists</td><td>Methods
Evidence review G
Evidence review D</td><td>020
Review G, 3.2.1.
Review D, Section 1.2.5.1 /59</td><td>008
313
1</td><td>The Dutch consortia looked at 8 Dutch randomised controlled trials, (6 of which are included in the review). With a combined total of 1310 patients, 90% of participants reported PEM. 77% of participants fulfilled the IOM 2015 criteria for SEID, which includes PEM. When the outcomes of the randomisation were looked at (699 CBT and 611 control), CBT still gave a significant advantage to fatigue (CIS) and disability (sf-36 physical functioning increase, SIP total score decrease). There was no significant interaction between treatment (CBT vs waiting list) and PEM at baseline, meaning PEM did not moderate the effect</td><td>Thank you for your comment.
PEM
The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence.</td></tr>
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				of CBT. So most patients meeting CDC criteria for CFS also report PEM. The subgroup of patients with PEM improved with CBT, and PEM does not moderate outcome in these trials of CBT versus waitlist controls, care as usual or natural history (1301 patients). Why is PEM give such prominence?	PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 D:	008	99% of the FINE trial participants were rated as having PEM https://doi.org/10.1186/1741-7015-4-9, , (Wearden pers com)	Thank you for your comment. *Reanalysis PEM* We looked for any published information on the percentage of participants with PEM in the included trials, or subgroup analyses in study participants with PEM. The papers for all included studies were reviewed again, as well as any published supplements. The excluded studies list was also re-examined to ensure any relevant information relating to PEM in the included studies were not missed. Unpublished data was not accepted for this analysis.

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The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	There was no reason why the Committee could not have asked for the data on rates of PEM in the trials that they knew would be subjected to the "indirectness" criteria. A call for evidence that was issued during the conduct of the Review, and this could easily have included within that. Was this ever considered, given the importance of the subject?	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence. *Reanalysis PEM*

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					We looked for any published information on the percentage of participants with PEM in the included trials, or subgroup analyses in study participants with PEM. The papers for all included studies were reviewed again, as well as any published supplements. The excluded studies list was also re-examined to ensure any relevant information relating to PEM in the included studies were not missed. Unpublished data was not accepted for this analysis.
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	Another recognised technique would have been to question whether or not the premise of the Committee, that there is no ME/CFS without PEM/PESE as it is currently defined or measured, is incorrect. There has been no systematic assessment of the validity and reliability of the symptom of PESE and at present there is no agreed definition, no agreed specification of what is 'exertion', no agreed specification of the temporal relationship to exertion, and no agreed definition of what counts as a 'symptom' or as an 'exacerbation' and a wide range of patient experiences grouped together under this umbrella https://doi.org/10.1371/journal.pone.0197811 Whilst there is research on the Two Day Cardiopulmonary Exercise Test (CPET)., the committee reviewed evidence showing that there was no consensus on this (Evidence Review B page 91, Davendorf) and did not make any recommendations on this. This lack of clarity has resulted in reliability problems; for example in Jason et al study (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4295644/) 8 out of 32 patients who had been scored as PEM negative, according to their self-endorsement of the CDC criteria symptoms, but	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness.

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				when this symptom was probed differently by the physician "all of the patients appeared to have PEM" Jason et al concluded that the existing measures were not sensitive enough for the detection of PEM; and the rates of PEM in studies using the CDC criteria may underestimate true rates of PEM, not overestimate them, which is the Committee's position. Nor is there evidence of how commonly it co-occurs with unrefreshing sleep and cognitive difficulties - the core criteria of NICE's new definition. So overall everyone accepts that PEM is common and important, but that does not mean it can treated as "pathognomonic". The evidence is just not strong enough to give it the important that the committee did. There remains considerable uncertainty. The symptom itself is not a single discrete entity, present or absent. It can be experienced in many different ways. It is difficult to measure operationally – it is a self-reported symptom, and is no clear "objective" test for PEM with good sensitivity or specificity to be used in this context, either back when the trials were done, or now. To place all one's eggs in the basket saying that those who have entered a study who may not have recorded PEM do not have ME/CFS seems very likely to be creating a risk of false negatives, people who actually do have ME/CFS, which the committee will later agree is a bad thing. Finally, the underpinning evidence review in the IOM criteria (IOM 2015 https://doi.org/10.17226/19012), on which the Committee have relied for their own version of its diagnostic criteria, reports varying rates of PESE in patients with ME/CFS from 69% to 86%, depending on how PESE was defined. They noted unrefreshing sleep to be present in 92% of cases, and cognitive difficulties in 50 to 80%, depending on definition used.	*After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population $\geq$ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

Myalgic encephalomyelitis (or encephalopathy)/chronic fatigue syndrome: diagnosis and management
Consultation on draft guideline - Stakeholder comments table

10 November 2020 - 22 December 2020

Stakeholder	Document	Page No	Line No	Comments	Developer's response
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	The Committee assume, without good evidence, that PESE is pathognomonic for ME/CFS. However, we contend that the evidence suggests otherwise (see below). The only way it becomes pathognomonic of ME/CFS is if they simply announce that it is - a clearly circular argument. Likewise, they assume that the measurement of PESE is so reliable that it is reasonable to insist that every patient in a trial must have recorded the presence of PESE. But the measurement of PESE has not been found to be reliable. They also assume that if it hasn't been recorded, then the patient hasn't experienced it, which again the evidence suggests is frequently not the case. So we contend that to jump from variations in the different ways in which PESE is treated in any given diagnostic system, none of which are a gold standard, to impute that there is a "serious risk of indirectness" with everything that implies, simply cannot be justified. Does NICE agree that there are sufficient problems in the measurement and recording of PESE to make the recommendation of "serious risk of indirectness" that was dependent on this unsafe?	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	008 313 1	Factor analysis of the predictive value of PEM in diagnosis of ME/CFS could have also have been considered. For example, Sullivan et al 2005 study of 5330 subjects from the Swedish twin registry with fatigue problems which using latent class analysis found a syndrome strongly resembling a ME/CFS like illness but found no evidence to support a particular diagnostic value in post exertional malaise (doi:10.1017/S0033291705005210). Does NICE agree that is evidence that does not support the view of the committee on indirectness. If not, why not?	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail).The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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					The paper by Sullivan examines a large population who were asked 'have you felt abnormally tired during the last 6 months?'. Those who said yes to the initial question were then asked the supplemental questions in the Fukuda criteria. The paper is essentially a critique of the Fukuda classification and specifically the 'requirement of four of eight cardinal CFS symptoms'. The results of the study 'suggest that the CDC-94 [Fukuda] criteria have fundamental flaws for the classification of fatigue in a population-based sample'. It is of note that the consultee describes the Fukuda Criteria as 'far and away the most cited criteria in CFS research'. The paper says nothing about the validity of PEM as one of the criteria for diagnosing ME/CFS
The Royal College of Psychiatrists	Methods Evidence review G Evidence review D	020 Review G, 3.2.1. Review D, Section 1.2.5.1 /59	8 313 001	The committee seem also to be under the impression that post exertional malaise/ symptom exacerbation is a unique symptom of ME/CFS. But this is untrue, it is commonly reported in other conditions; for example in the context of fatigue associated with major depressive disorder (http://europepmc.org/article/med/20035251), multiple sclerosis (doi: 10.1097/PSY.0b013e31824152ed), stroke (Staub, F., Annoni, J.M. and Bogousslavsky, J., 2000. fatigue after stroke, Cerebrovasc Dis, 10(suppl 2), p.62), traumatic brain injury (doi: 10.4085/1062-6050-48.5.02), cancer (doi.org/10.1016/j.jpainsymman.2020.02.012), gulf war syndrome (doi.org/10.1016/j.ijpsycho.2019.11.008) and indeed it has even been reported in 8% of healthy sedentary adults (IOM 2015 full report DOI 10.17226/19012) Importantly PESE is particularly present in the related condition of fibromyalgia (https://pubmed.ncbi.nlm.nih.gov/8092909/), which has considerable overlaps with ME/CFS. There is overlap in the literature, overlap in the clinic, and overlap in the community. It is often just a matter of chance or local resources whether a patient with similar symptoms is referred to rheumatology and received a diagnosis of fibromyalgia, or an	Thank you for your comment. Based on the evidence (Evidence review D) and the committee's clinical experience, they agreed the four criteria for the diagnosis of ME/CFS were fatigue, post-exertional malaise, unrefreshing sleep and sleep disturbance (or both), and cognitive difficulties. Key to the diagnosis of ME/CFS is the presence and combination of the four symptoms. The committee have not suggested that any of these symptoms are individually unique to ME/CFS. The fact that central chest pain can occur in oesophagitis does not mean that it is not a feature of myocardial infarction. Thus, pain may be associated but is not exclusive to with ME/CFS, and this was supported by the IOM diagnostic criteria (2015). The committee note that pain is the dominant symptom in fibromyalgia and as such the two populations are differentiated. The committee agreed that the recommendations in sections 1.1 and 1.2 for all types of chronic pain in the Chronic pain guideline could apply to people with ME/CFS but that the population ' chronic primary pain' is a different population to that of people

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				CFS service receiving a diagnosis of ME/CFS. Lots of support groups around the world welcome members with either. Yet as we have already pointed out, the NICE Guideline that includes fibromyalgia (Chronic Pain) in its current draft form recommends both exercise and cognitive behavioural therapies as appropriate treatments. What does NICE intend to do about this inconsistency?	with ME/CFS and that the management section does not apply. As such the difference between the guidelines is not a problem. The committee made the decision not to cross-refer to the chronic pain guideline to avoid confusion.
The Royal College of Psychiatrists	Methods	021	013 - 106	"*The committee agreed that some diagnostic criteria that have been used in the past may not accurately identify an ME/CFS population and it is likely that the use of such criteria has resulted in people misdiagnosed as having ME/CFS being included in the studies.*" To make such an important decision (to downgrade all trials that did not mandate PEM in their illness definitions), which drastically reduces the evidence base, requires evidence, not simply opinion. And there is no reliable evidence to show that patients recruited to trials using either the CDC or Oxford criteria do not have ME/CFS. Devasahayan et al (2010; https://doi.org/10.1258%2Fshorts.2010.010042) showed that trials that use these criteria are better at picking up comorbid conditions than clinicians by themselves. Trials use standardised assessments to exclude patients with either physical or mental health disorders that better explain symptoms in people suspected of having ME/CFS. Could NICE comment please?	Thank you for your comment. The evidence base is not reduced by the decision to downgrade studies that did not include PEM as an essential criteria. Evidence from such studies was not excluded or dismissed but was downgraded, reflecting a common criticism that the criteria used in such studies are too broad. The comment that 'there is no reliable evidence to show that patients recruited to trials using either the CDC or Oxford criteria do not have ME/CFS' is circular, and does not negate the committees view that the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness (see evidence review D for further detail). The reference to Devasahayan (sic) is, we suspect, to Devasahayam A, Lawn T, Murphy M, White PD. Alternative Diagnoses to Chronic Fatigue Syndrome in Referrals to a Specialist Service: Service Evaluation Survey. *JRSM Short Reports*. 2012;3(1):1-5. doi:10.1258/shorts.2011.011127. The doi reference given links to Lawn T, Kumar P, Knight B, Sharpe M, White PD. Psychiatric misdiagnoses in patients with chronic fatigue syndrome. JRSM Short Reports. 2010;1(4):1-7. doi:10.1258/shorts.2010.010042. These studies looked at errors in referral (Devasahayam 2012) or the detection of co-morbid psychiatric diagnoses (Lawn 2010) in CFS/ME patients referred to a specialist ME/CFS clinic. Neither paper supports the thesis that trials that use the CDC or Oxford criteria are better at picking up comorbid conditions than clinicians by themselves.

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The Royal College of Psychiatrists	Methods	021	016 - 021	"*Post-exertional symptom exacerbation was identified as central to the diagnosis of ME/CFS and the committee noted that some criteria have not included this as a compulsory requirement. The inclusion of non-cases may have obscured the true effect of the different interventions on people with ME/CFS and this raised concerns over the generalisability of findings to the wider ME/CFS population*." Where is the evidence that PESE is central – or indeed essential – to the diagnosis of ME/CFS? PEM occurs in many conditions, not just CFS/ME, such as fibromyalgia and mild traumatic brain injury, so is not pathognomonic for ME/CFS. The PACE trial showed that participants who met the London criteria for ME (which requires PEM) were no different in their response to CBT and GET than those who met other criteria (White et al, 2011, cited above). Since this decision was crucial in down-grading 27/30 RCTs of both CBT and GET, and also led to excluding the Cochrane reviews of CBT and exercise therapies, Could NICE please reconsider this far-reaching decision, and update the evidence reviews accordingly.	Thank you for your comment. PEM The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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					London criteria The London Criteria as used in the PACE trial ('PACE trial protocol: Final version 5.0, 01.02.2006 p188) does not include post exertional malaise. On the basis of the written criteria used to assess participants in the PACE trial the committee could not establish that participants experienced post exertional malaise.
The Royal College of Psychiatrists	Methods	021	012	We were surprised to see that an outcome question had already been decided in the methods prior to the search for evidence. This seems a major methodological flaw- "indirectness was important to take consider. The committee considered the diagnostic criteria used in the studies to recruit eligible participants. The committee agreed that some diagnostic criteria that have been used in the past may not accurately identify an ME/CFS population and it is likely that the use of such criteria has resulted in people misdiagnosed as having ME/CFS being included in the studies. Post-exertional symptom exacerbation was identified as central to the diagnosis of ME/CFS and the committee noted that some criteria have not included this as a compulsory requirement" The accuracy of post exertional symptom exacerbation (PESE) as a diagnostic symptom clearly falls within the remit of the questions for the review as specified in table 2 page 6 methods review. We note the absence of any supporting evidencefor this statement and would like NICE to explain how this decision was justified.	Thank you for your comment. The review question 'In people with suspected ME/CFS, what are the criteria used to establish a diagnosis?' was one of the first that the committee examined. A descriptive methodology was used to establish the recommended criteria and this is well described in evidence review D. The committee acknowledged there is an ongoing discussion in the ME/CFS community about which diagnostic criteria are best and which should be used in the identification and diagnosis of ME/CFS. The factors influencing these discussions are the broadness of the inclusion criteria, the definition of some of the symptoms, and the usability of the criteria as a clinical tool. On the basis of this, the committee determined that people with ME/CFS should have all of the following: debilitating fatiguability, post-exertional symptom-exacerbation, unrefreshing sleep and cognitive difficulties. It is also of note that many other diagnostic criteria for ME/CFS have been made by 'expert committees' or 'working groups' specifically established for the purpose, including the Oxford Criteria, which arose from a 'a meeting of research workers with a known interest in the field' (Sharpe 1991)'.
The Royal College of Psychiatrists	Methods	021	021	"The committee agreed to downgrade evidence for population indirectness where studies used diagnostic criteria for entry that do not include Post-Exertional Symptom Exacerbation as an essential symptom. This included the CDC 1994 criteria, upon	Thank you for your comment. No trials were excluded that met the protocol inclusion criteria. PEM

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				which the majority of the evidence was based, as well as the CDC 1988 and Oxford criteria". We are concerned at the lack of evidence to support this decision which excludes around 80-90% of the available evidenceon treatments. The committee found no evidenceto prioritise one set of criteria over another nor did they find any evidence to prioritise any specific symptom. In particular they found no evidence to prioritise post exertional symptom exacerbation. They openly acknowledge that they took this decision on the sole grounds that they thought Post-Exertional Symptom Exacerbation fitted their experience. This is highly concerning as this decision effectively renders the guideline scientifically void as the overwhelming majority of the scientific literature used the downgraded definitions. Some 80 to 90% of available trials are consequently excluded from the analysis and it prevents NICE considering systematic reviews and meta-analyses from the Cochrane Collaboration. Trials which present the prevalence of PEM/PESE at baseline show that between 84 and 100% of patients meeting the now banned criteria have PEM. The largest trial (PACE) actually used PEM as a secondary outcome and showed that PEM remitted more with graded exercise therapy and CBT more than pacing therapy and specialist medical care (see DOI:10.1016/S0140-6736(11)60096-2). By making this arbitrary decision, the committee has missed the opportunity to establish which treatments if any help this important symptom. If the committee had found a clear scientific basis for this decision, then it could potentially be justified. In the absence of any supporting evidence it must be reconsidered. We also consider there to be an ethical dimension to this decision. The patients, who consented to be randomised in the now excluded trails, did so on the grounds that these were publicly funded trails that had been rigorously assessed and prioritised by national funding bodies and the knowledge gained would help the common good. To discount their data and their efforts, without any scientific basis, is a breach of trust between NICE and the participating patients.	The committee emphasised it is the combination and interaction of the symptoms particularly with the addition of PEM that is critical in distinguishing ME/CFS from other conditions and illness. (see evidence review D for further detail). The committee considered that the response to an intervention is likely to be different in people who have PEM compared to those who do not, and this should be taken into account when interpreting the evidence. PEM is widely acknowledged in specialist ME/CFS practice as being a characteristic feature of ME/CFS. The difficulty for interpreting the evidence is that in the trials that do not use a criteria that has PEM as essential (and therefore a 100% ME/CFS population) numbers of people with PEM are rarely reported . The committee do not assume that people recruited to trials do not experience PEM they just don't know how many if the information is not reported. To address this the committee agreed that evidence without this information would be 'indirect' acknowledging this uncertainty*. As such the evidence was considered taking this into account. See the methods chapter for more information on GRADE and indirectness. *After considering the stakeholder comments the committee agreed to revisit the evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.

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The Royal College of Psychiatrists	Methods	026 027 028	007 – 023 001 - 039 001 - 010	It does not appear as though the same quality standard regarding indirectness (i.e. PEM being mandatory) was applied to the qualitative studies, as were applied to the quantitative studies, such as the RCTs. Why was this double standard applied? Since the committee relied heavily on the qualitative data regarding the harms of GET, this is an important issue, which undermines the confidence in the impartiality of interpretations applied to the evidence as a whole.	Thank you for your comment. After considering the stakeholder comments the committee agreed to revisit the quantitative and qualitative evidence for the intervention reviews further scrutinising the information on PEM reported in the trials and the application of indirectness and relevance in the evidence. As part of this they agreed that any quantitative and qualitative evidence with a population ≥ 95% with PEM would be considered direct. See evidence review H appendices G and F for the approach taken, the analysis and the impact on the results and interpretation of the evidence.
The Royal College of Psychiatrists	Methods	028 022 023	030 - 031 & table 12 31-32 13-16	The PACE trial determined what an MCID and clinical useful difference (CUD) should be for the primary outcomes of fatigue and physical function in adults, a priori, before examining any outcome data – and reported it in main paper and the published statistical analysis plan. The PACE trial choices were guided by Guyatt GH, et al. Methods to explain the clinical significance of health status measures. Mayo Clinic Proceedings 2002; 77: 371–83 and by Cohen J. Statistical Power Analysis for the Behavioral Sciences.2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988. The MCID was calculated as 0.3 standard deviation of pooled baseline on primary outcomes, and the CUD was calculated as 0.5 of the standard deviation of the pooled baseline data on primary outcomes. The CUD translated to 2 points on the Chalder Fatigue Scale and 8 points on the SF36 physical function scale. See attached stats analysis section in White, 2011 and page 17 of Walwyn et al. White et al, 2011, https://doi.org/10.1016/S0140-6736(11)60096-2; Walwyn et al, 2013, http://www.trialsjournal.com/content/14/1/386. Figures for the SF36 were also available for other medical conditions, to show that a score of 8 points is consistent with the	Thank you for your comment. All NICE guidelines follow the process for evidence reviews as set out in Developing NICE guidelines: the manual. This guideline was no exception. The review protocol is developed by the review team and the guideline committee. The review protocols were drafted by the reviewing team and then refined and agreed with the committee members. This included discussion on MIDs and the committee agreed in the absence of any published and accepted MIDs to use the default MIDs proposed by the GRADE working group (see the methods chapter for more detail).

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				wider literature (Moehli et al, 2020 https://doi.org/10.1186/s12955-020-01344-w). A MID of 0.5 of the median of standard deviations in meta-analyses conducted would be equivalent to a moderate not minimal effect size, according to Cohen (cited above). Why were these figures not used by the review team, since they found no others that applied to adults? We suggest a revision of the pertinent reviews to incorporate these thresholds for adults please.	
The Royal College of Psychiatrists	Methods	032	040 - 044	"*The committee considered the appropriate 'strength' of each recommendation. This takes into account the quality of the evidence but is conceptually different. Some recommendations are 'strong' in that the committee believes that the vast majority of healthcare and other professionals and patients would choose a particular intervention if they considered the evidence in the same way that the committee has.*" What evidence did the reviews and committee consider to support these beliefs? We were surprised that published studies of the patients attending NHS secondary care services in the UK were not considered. See: Crawley et al, 2013, https://doi.org/10.1093/qjmed/hct061 and Collin et al, 2017 https://doi.org/10.1186/s12913-017-2437-3 - about a third of patients rated themselves "much" or "very much" better. Added to this should have been views of the 3659 participants of CBT and GET trials. For instance, 88% of participants were satisfied with GET, compared to only 1% dissatisfied in the PACE trial (White et al, 2011, cited above). For CBT in the same trial, 82% were satisfied compared to 5% dissatisfied. Why were these available data not considered by the committee?	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE

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					guidelines: the manual, section 9.1 for further details on how recommendations are developed). Neither of the studies met the inclusion criteria for the intervention protocols. Both are non-comparative.
The Royal College of Psychiatrists	Question from comments form	1		1 Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. Specialist services in the NHS, and internationally, have for many years provided both graded exercise therapy and cognitive behaviour therapy for patients with ME/CFS. They have done this because these are the treatments for which there is best evidence of efficacy in trials and because clinical audits, both published and unpublished, and clinic patient surveys have confirmed both the effectiveness of and satisfaction with these two treatments They have also provided these two treatments in the knowledge of their safety, provided that they are prescribed in the appropriate way by properly trained and supervised therapists, with knowledge of the illness, working with each individual in patient centred collaboration They have also provided these treatments because many patients have wanted them. Not being able to provide these as treatments for ME/CFS for their patients will have a fundamentally negative effect on what treatments these services can provide. There will be no evidence based treatments available for these services to provide and for their patients to access. Furthermore clinical commissioning groups will regard these services as only providing "Procedures of Limited Clinical Effectiveness (PoLCE)". See: https://www.england.nhs.uk/evidence-based-interventions/interventions/. This is because there is little or no evidence to support NICE's recommendations, such as self-	Thank you for your comment and information. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). The guideline continues to recommend CBT and the wording of this recommendation is now less negative in tone. The PoLCE initiative that you refer to relates only to procedures, not to therapies. Its rationale is to prevent harm to patients, and this has also been a driving force behind this guideline. The committee are clear that this guideline is based on the broad evidence base and are confident that commissioners will demand these services.

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				management based on the principle of energy management. This will inevitably lead to decommissioning of specialist services for patients with ME/CFS.	
The Royal College of Psychiatrists	Scope	008	Para 3.6	The scoping document outline eight main outcomes to be considered, which does not include mortality. Why was mortality added later as a critical outcome when the mortality for natural deaths is probably the same as the general population? (Carr et al, 2019, https://doi.org/10.1017/S0033291719001065). If it was added because of the risk of death by suicide why is there not more guidance on assessment of comorbid psychiatric disorders and suicide risk? (Roberts et al, 2016 http://dx.doi.org/10.1016/S0140-6736(15)01223-4)	Thank you for your comment. When developing the protocols for the evidence reviews the committee agreed that mortality was an important outcome to measure when evaluating interventions. This is a standard measure to include when assessing the clinical and cost effectiveness of an intervention.
University College London Hospital NHS Foundation Trust - TRACCS	Appendix 1 - Children and Young People	General	General	We are really grateful for the effort made to include the voice of children and young people (CYP) with ME/CFS. This is essential to ensure we can deliver meaningful, good quality care to our patient cohort. However, we are concerned that more was not made of the methodology noting that the group was very homogenous (which is not our experience of ME/CFS sufferers) and there is a risk to the generalisability of the YP voice when recruiting patients through a single organisation.	Thank you for your comment. In Appendix 1 the study authors set out the limitations of the consultation and acknowledge the limitations on recruitment and the representation of the sample. Despite limitations in recruitment (small sample, lack of involvement of third-party organisations), the sample was heterogenous in that it included a range of geographies across England, genders and condition severities (CYP reporting ME/CFS severity ranging from mild to severe did take part). Section 4 of Appendix 1 describes the committee's overview of the consultation. In this they noted it was unclear if all the sample were recruited from Action for ME potentially representing only one group of young people with similar views and if the participants were currently under NHS care and if the experiences reflected current care. This was taken into account in the committee's decision making when considering how this contributed to the body of evidence and when making the recommendations. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a

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					range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The committee included members with clinical and personal experience of children and young people with ME/CFS. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. In the case of children and young people the themes and findings in the commissioned report were reflected in the qualitative reviews across the guideline. The populations in the majority of studies included in the qualitative evidence was described as mild and moderate ME/CFS. As with all NICE guidelines the committee members used their experience and judgement to interpret the evidence and then through discussion and deliberation, the committee agreed what it meant in the context of the topic to make recommendations. (See Developing NICE guidelines: the manual section 9.1 for further details on how recommendations are developed).
University College London Hospital NHS Foundation Trust - TRACCS	Appendix 1 - Children and Young People	017	004 - 005	Supporting Child and Young People document (Appendix 1) line 4-5 p17 The data from the survey of the 16 children and young people surveyed indicated that they want to know 'how to get better and feel better' and that experiences of this were highly valued. The guidance offers clear ways in which severe and very severe patients are affected but has no examples of those with mild to moderate symptoms. This may be overwhelming for children and young people or any newly diagnosed patients who do not see themselves in this experience.	Thank you for your comment. After taking into consideration the comments from stakeholders the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor would this section be mistaken to reflect the experience of all people with ME/CFS. In addition the committee

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					reviewed all the recommendations and edited those they agreed had a focus on severity. These recommendations included the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.).
University College London Hospital NHS Foundation Trust - TRACCS	Appendix 3 - Expert testimonies	General	General	The points made that graded exercise therapy is now such a weighted term that use of it in the NICE guidance would be inflammatory are fair. However, the usual practice of GET by trained physiotherapists is adapted to different patients rather than an automatically fixed programme. Perhaps a more open discussion around why GET has been advised as "do not offer" would be helpful with the reasoning of the committee more explicitly spelled out.	Thank you for your comment. See evidence review G- non pharmacological management for the evidence and detailed committee discussion about physical activity and graded exercise therapy.
University College London Hospital NHS Foundation Trust - TRACCS	Equality impact assessment	General	General	We note that the committee could not make significant note of where this guidance may have impact on equality. We can see a number of areas where equity is lacking or problematic within ME/CFS diagnosis/treatment and where the committee may be able to flag this to improve outcomes. 1. The recent NHS equality and racism 2020 review noted that racism is inherent in medical management and diagnosis. This is true in ME/CFS with harmful stereotypes around different ethnic groups being perceived as lazy, or prone to complaints of body pain. It is therefore likely that patients from Black and Minority ethnic groups may be less likely to receive a diagnosis of ME/CFS and therefore miss out on treatments that would improve their outcomes and subsequent quality of life. Not treating or diagnosing patients effectively means the impact ME/CFS has on ability to gain	Thank you for your comments. An equality impact assessment (EIA) has been completed for this guideline and is available on the guideline webpage. When evaluating all the evidence the committee considered all the groups identified in the EIA, the applicability and generalisability of the evidence was considered by the committee in their discussion of the evidence. Very little specific evidence was identified for any of the groups and the committee agreed that the recommendations should equally apply to all groups and did not discriminate against any particular group and separate recommendations were not thought necessary for any of these groups. The committee agree these factors need to be considered when delivering care and have added, 'be sensitive to the person's socioeconomic, cultural and ethnic background, beliefs and values, and their gender identity and sexual orientation, and think about how these might influence their experience, understanding and choice of management'. *Recommendations for research*

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				qualifications and engage with employment perpetuates any socioeconomic difficulties already increased in BAME groups. 2. We know there is an under-representation of lower socio-economic groups in ME/CFS clinics, and yet the disease is not less common in these groups* 3. It should also be noted that systemic inequalities result in increased risk of long-term conditions, worse care, and worse outcomes for different groups. We should all be alert to this possibility, especially as more articulate patients (and particularly parents) are able to navigate a complex system; ask for more advocacy around education, support and adjustments in school and college; and are likely to be more confident in asking for specialist care and contacting the "named" professional who (pg 23 ln 7-10) would be able to help make adjustments needed to maximise care & outcomes. This will have an impact on outcomes and care received across the social demographic gradient and is not equitable. 4. We think it should be noted that in a condition where there are a number of alternative therapies and private consulting groups targeting patients with the diagnosis, or where confusion lies that this can be a problem as patients are taken advantage of. In the call for easier referral and more specialist input – it is important to know and understand who may be able to benefit from this the most and try to mitigate for this openly.	To raise awareness of this gap in the evidence pregnant women and women in the post-natal period, black, Asian and ethnic minority populations have been specified in the population for the self-management strategies, sleep management strategies, and dietary strategies research recommendations. Point 4. The committee agreed it was important to raise awareness about the current lack of a cure for ME/CFS and made a recommendation to address this. They noted in the rationale for managing ME/CFS that they were aware of claims that have been made about cures for ME/CFS and that there is often a financial cost to people with ME/CFS when they pursue these.

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				Any NICE guidance absolutely has an explicit role in this. * Francesca K Neale, Edward J Armstrong, Jonathan M Cohen, Terry Y Segal, Dougal S Hargreaves How fair is our service? Evaluating access to specialist paediatric care Archives of Disease in Childhood Nov 2019, 104 (11) 1105-1107; DOI: 10.1136/archdischild-2019-317254	
University College London Hospital NHS Foundation Trust - TRACCS	Evidence review G	General	General	Evidence – it appears that outcomes for children and young people (CYP) are different. Additionally, they are going through changes in neurodevelopment and this would be in keeping with the understanding of what, as the guidance says, is classified as a neurological condition by the WHO and the UK. Therefore evidence review is lacking on CYP data and recommendations for adults should be considered with care in children. There should be a specific call for more CYP data. 4 studies in evidence review 7 were specific to CYP, with 4-5 more with data including 15/16yo (but not separating them out). The evidence from these studies was considered to be of low or very low quality due to concerns over bias – Professor Jonathan Edwards, UCLH, expresses concerns in his professional testimony about lack of blinding in these trials. This is reasonable, however, we also note the recent BMJ article * questioning some of the literature review methodology and would ask for the guidance to be more open about what evidence is available; where it comes from; and how it can be applied to practice in an evidence based manner where the peer-reviewed literature is applied on a patient by patient basis, and constantly reviewed alongside the patient with their views and values , and the clinicians experience all used for decision making. We would be grateful to the committee for their	Thank you for your comment. The committee agree that there was limited evidence in children and young people. Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. Children and young people have been included as population of interest in the research recommendations. *Methodology* All NICE guidelines follow the process for evidence synthesis set out in Developing NICE guidelines: the manual. This guideline was no exception. When developing this guideline the committee considered a wide range of evidence, including that from published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature, including children and young people. *Harms/ adverse events*

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				research recommendations proactively moving these conversations forward. Of note, the evidence of harm on which NICE recommendations are made are also taken from studies, or even from discussion with patients (as noted by Dr Jonathan Edwards himself acting in the same way and basing some of his concerns on interactions with ME/CFS patients). No harm is noted in the studies themselves, but on discussion around the studies. This could call into question the validity of calling one group of studies low quality evidence but relying on another group of studies (or personal experience/conversations) to make recommendations that have similar problems. <u>We would therefore like the committee to recommend specifically that CYP need further research into long term outcomes generally, impact of different management strategies.</u> *Turner-Stokes, L & Wade, D T. Editorials: Updated NICE guidance on chronic fatigue syndrome. BMJ 2020; 371	The committee agree there needs to be better reporting and long-term data collection of harms in RCTs. The difficulties with the collection, analysis and reporting of adverse events in randomised controlled trials is not disputed (for example see https://bmjopen.bmj.com/content/9/2/e024537). Notwithstanding this, it is important that a comprehensive approach is taken to understanding the impact of any intervention when implemented in research trials and in practice. Ideally this takes both a quantitative and qualitative approach and includes the experiences and opinions of all people who have had the intervention, patient experience is invaluable. As with all NICE guidelines the committee uses its judgment to decide what all the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	We respond to this guidance as a specialist ME/CFS service for Children and Young people (CYP) with a Multidisciplinary team encompassing medical and nursing staff, occupational therapy, physiotherapy, psychology, education, social care and administrative staff . The team are really pleased to see that Children and Young People are specifically mentioned in the guidance and treated as a separate group. This is great progress since the 2007 guidance. Overall however, we have some concerns about the way information for this group is framed and feel that CYP would benefit from either a separate part of the guidance (rather than following on from adult) or separate guidance.	Thank you for your comment and information. The committee discussed the comments on the format of the guideline and if the recommendations on children and young people should be in a separate section. They agreed that the recommendations mostly supplemented the other recommendations (for example, additional principles of care for children and young people) and that these key messages on care could be lost if there was a separate section on children and young people.

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				Our patients are a group with individual characteristics and demographics and have a range of difficulties and co-morbidities. Healthy adolescent neurodevelopment includes education and social interactions. We think it would be beneficial if the CYP sections specifically address these issues for YP in a way that can be encouraging and empowering to them and provide an approach to a safe increase in activity over time. Many young people we see were highly active before they had ME/CFS and their ambition is to return to a full and active life (like many adults). It would be a helpful addition to include guidance for those people who want to engage in lots of physical activities and discuss the role of hope and aims. Some discussion of an approach to increasing a young person's baseline should be within the guidance and it be noted that the reason for engagement with specialist services is to look at how to do this sensibly and gradually, rather than focusing on the harms of thinking of, or approaching, exercise & activity	Children and young people are named as a group for special consideration in the scope and with every recommendation the committee considered if the evidence was applicable to children and young people and then if different or additional recommendations were appropriate. Where this was the case separate recommendations were made. The committee agreed that the recommendations on energy management, physical activity and exercise applied to children and young people. Included in these are recommendations on a safe approach to increasing activity. Throughout the guideline the importance of ME/CFS specialist services is reinforced and where access to these services is required. The management section of the guideline sets out the interventions for supporting people with ME/CFS to manage their symptoms, including if appropriate programmes for physical activity and exercise.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	Terminology: Whilst we appreciate how some terms are considered to be better by the committee, matching them alongside known terms (particularly if a patient were to use a search engine to look up management plans) would be helpful. Removing pacing, baseline, activity over and under management (or boom and bust) may be confusing. We understand that the use of the term deconditioning has been used inappropriately with patients with ME/CFS as an explanation for why they developed the condition. However, in any condition where activity levels are reduced beyond a certain baseline, deconditioning can occur. This is not the same as saying that the original cause of ME/CFS or a major contributing factor to its ongoing nature are due to	Thank you for your comment. The committee agree that there are many different terms used across the ME/CFS research, clinical and patient communities and the committee have taken care to define the ones used in the guideline. The committee discussed the use of the term pacing agreed that it means something different to different people with many versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it. After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to change the following terms:

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				deconditioning, but it is still the case that deconditioning is likely to occur. If previous guidance overstated the role of deconditioning, this should be addressed, but it is not accurate or appropriate to remove it completely. We have a number of patients with orthostatic conditions and hypermobility where deconditioning can lead to an increase in symptoms. The impact of reduced physical activity in this group is not explicitly noted in the guidance, and it would be helpful to discuss the aim of achieving a balance between ME/CFS and these other conditions more explicitly in the guidance. Again if this is considered a term the guidance is keen to avoid, it should still be made clear in the guidance the impact reduced physical activity has on any person with any condition.	• Energy envelope to energy limits. The committee noted the concept of describing the amount of energy a person has to do all activities without triggering an increase in their symptoms remains the same. • Debilitating fatigability. This has been changed to be more descriptive of people with ME/CFS, 'Debilitating fatigue that is worsened by activity, is not caused by excessive cognitive, physical, emotional or social exertion and is not significantly relieved by rest.' • Post exertional symptom exacerbation (PESE) to Post exertional malaise (PEM). The committee recognised PEM is an equivalent term that is more commonly used and there was not strong support in the stakeholder comments to use the term PESE. In the discussion section of Evidence review D the committee outline why the term PESE better describes the impact of exertion on people with ME/CFS. *Deconditioning* In the physical functioning and mobility section of the guideline the committee recommend that strategies to maintain and prevent the deterioration of physical functioning and mobility are included in the care and support plans for people with ME/CFS. Taking into account the range of stakeholder comments, ' as the cause of ME/CFS' has been deleted from the recommendation and replaced with 'perpetuating ME/CFS'.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	Language: As a team we all noted the change in tone on this guidance in comparison to 2007 where sentences were shorter, and the differences in expert opinion, lack of evidence base and confusion for professionals, patients and families alike was noted and acknowledged. We feel that guidance left room for individualised, bespoke, holistic, kind and considerate patient care to be the forefront.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to develop recommendations that were individualised but reflected the variation in the impact and severity of symptoms that people with ME/CFS experience. After taking into consideration the comments from stakeholders about

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				We note that the guidance implies in a number of areas that patients rarely recover (p14, 22-24) and there is no treatment or cure (p24, 4-5.) Unfortunately the nocebo effect also exists, and the tone of this guidance could have this influence on patients and families. No matter the diagnosis, and its prognosis, it is not routine for clinicians to take all hope away from patients and families. Other NICE guidance for chronic conditions without a cure (such as tinnitus) move away from a negative tone or focus on lack of cure and focus instead on "quality of life" and "management strategies for living better". The removal of hope of recovery is likely to increase low mood and anxiety and decrease chance of recovery.	the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). *Cure* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	We are aware that there have been a number of articles and interest on social media with relation to this change in guidance. Opinions have been split and we understand some of the debate has been fraught. We would therefore ask that the tone of the guidance appreciate this. Three areas give rise to concern here. Firstly, that the negative tone relating to long-term outcomes allows for short statements to be made that may induce fear in patients and families. The second areas of concern are that didactic points of guidance around a topic for which the committee itself has	Thank you for your comment. *Tone of the guideline* When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and

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				concluded there is not strong evidence in either direction. We recommend that it would be helpful to acknowledge this more openly in the guidance (as with the 2007 guidance) rather than directing people to long evidence review documents most are unlikely to read. This may reduce the contentiousness around the release of new guidance. Finally, we are concerned that the subsequent finer detail of the guidance may be missed. (Often negative starting statements such as pg 27 "do not offer" are followed by more information that clarifies the statement.) The nature of short social media posts is that the subtle points of the guidance would be missed and flame an argument that is inappropriately didactic. With this in mind we would also ask for the committee to consider some of the short phrases that may be used on social media or sites as direct quotes from the guidance. For example – the Do Not Offer from page 27 may make an easy tweet, but if the guidance started with what was available and recommended, and then finished on what not to do, this may help people read the full guidance. We would be grateful if the implications for how the guidance is written could be considered with regard to how that impacts the: - Development of an individualised management plan - Interactions with patients and their families who have been reading social media - The interpretation of what a service offers including educational resources that may use terminology that is no longer deemed appropriate Managing expectations of patients, family and staff	edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. NICE guidelines have a different format to those published in 2007. In current guidelines the rationale section of the guideline sets out the key points of the committee decision making and then links to the evidence reviews.
University College London	Guideline	General	General	We find the approach of the guidance to management of the condition very negative and are concerned about the impact this will have on all patients who become fearful and further	Thank you for your comment. *Tone of the guideline*

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Hospital NHS Foundation Trust - TRACCS				reduce and restrict their activity inappropriately. It regularly says what should not be done and also indicates nothing is curative or is deemed to be treatment. It creates an impression that ME/CFS is a chronic almost irreversible life-long disability rather than a long-term illness that can and does improve for a proportion of people. The difficulty with this is that if there are no treatments, then we are confused as to the definition of what the recommendations are and would appreciate the committee expanding or providing a definition of treatment.	When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). . In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
University College London Hospital NHS	Guideline	General	General	The introduction for the 2007 guideline provided some helpful context to ME/CFS. A new version of this with updated figures would be helpful.	Thank you for your comment. The introduction section has been replaced with the context section at the back of the guideline and includes background

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Foundation Trust - TRACCS					information. The context is not intended to be exhaustive and sets the scene for developing the guideline. After considering the stakeholder comments some edits have been made to this section and the committee hope this adds some clarity.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	We understand patients have had negative experiences in the past of ME/CFS being dismissed as "all in the head", or 'psychological' or their fault in some way, and that is wrong and should in no way be perpetuated by uninformed medical professionals. However, it is important that there is the space and flexibility to open up discussions about the biopsychosocial aetiology and effect of any condition that includes fatigue and pain, or any other long-term condition. The impact on psychological well-being of living with any chronic health condition is widely documented and it is important that children and young people (CYP) living with ME/CFS should be able to access psychological support if they need/want it. Understanding the nature of symptoms and impact, on mood and lifestyle is essential for patients to feel in control of their care and decision making. A substantial minority of young people with ME/CFS also meet the criteria for co-morbid mental health problems, particularly depression and anxiety (Bould et al., 2011; Loades et al., 2017, 2020). In adolescents with chronic fatigue after Epstein Barr virus, fatigue severity was found to be associated with concurrent anxiety and with subsequent depression (Pedersen et al., 2019). We welcome that guideline signposts to the NICE guidance for treating anxiety and depression, but urge a note of caution about adaptations that may need to be made for someone living with ME/CFS (as that guidance has sections on exercise etc.)	Thank you for your comment. *Co-morbid mental health conditions* After taking into consideration the stakeholder comments the committee have revised the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders. The managing co-existing conditions of section of the guideline raises awareness that other conditions may commonly coexist with ME/CFS and these should be investigated and managed in accordance with best practice. This section also lists related NICE guidelines and recommends the section on principles of care for people with ME/CFS, section on access to care and the energy management recommendations should be take into account when managing coexisting conditions in people with ME/CFS. *Training* The committee agree that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. is beyond the remit of NICE to recommend what should be included in medical curriculum.

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				We would agree professionals require more training and education around this and we advocate for more input around the condition in medical school and training for professionals from different disciplines.	
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	The committee's recommendations being based on personal experience and expert knowledge is understandable given the evidence reviews and concerns over the Cochrane reviews resulting in a paucity of evidence. However, we would then suggest this is made more explicitly clear in the guidance or that more flexibility is introduced with regard to possible management. It is also contrary to the whole tone of the document which is that evidence does not exist that could lead to positive recommendations of treatments, but the committee go ahead and recommend things that have worked in their practice and personally. This is a contradiction and appears directly to conflict with the original aim of the NICE guidance review to be robust in its recommendations on the grounds of the quality of evidence. It is the experience of a few individuals and not representative of all those treating this condition who may have more positive experiences of recovery	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. This committee had a balance of perspectives and experiences. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). In current guidelines the rationale section of the guideline sets out the key points of the committee decision making and then links to the evidence reviews.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	General	General	We are concerned about the contradiction in the guidance; on the one hand the committee frequently mention that improved services and specialist input would lead to improved care, however the guidance explicitly says there is no treatment or cure for CFS and there is no explicit evidence that these changes would change outcomes.	Thank you for your comment. After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for symptom management for people with ME/CFS. However while the committee agree people with ME/CFS can manage their symptoms there isn't currently a cure for ME/CFS and it is important that people with ME/CFS are aware of this. Their discussion of how the evidence informed the recommendations is detailed briefly in the rationales in the guideline and in more detail in the discussion of the evidence sections in the review chapters.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	047 - 072	007 onwards	We read with interest the rationale for recommendations. We note how frequently the committee drew on their own knowledge and experience and the influence this group of people have therefore had over guidance for a condition on which you have established there is minimal high-quality evidence, and even the Cochrane reviews, so frequently considered exemplars of evidence collection and review, have come into question. We welcome the opportunity this review of evidence and guidance has given us as a team to look at our own practice, look to audit our own outcomes, discuss what the current evidence base is and the flaws within it when considering our own current practice alongside this new draft guidance.	Thank you for your comment. One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors

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					including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed).
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	024 - 029	General	The guidance here appears to become quite didactic and yet confused with mixed messages around physical maintenance, physical activity and structured or unstructured exercise. It would therefore be helpful to clarify this more within the scope of the guidance. We would recommend a shorter overview of the physical elements of managing ME/CFS before going into more detail. It is a really confusing section and has taken multiple readings to try and understand the main message. We provide more detailed points below. There is a generalization around physical activity and exercise that lacks detail. Different types of activity have significantly different energy loads (e.g., gentle stretches versus aerobic activity) and this requires clarification around increasing and increments – be this in duration of time or intensity. The implication taken from this guidance is that exercise is bad, and we think that this is unhelpful and restrictive to patients who want to try and do more whilst being supported.	Thank you for your comment. After reviewing the evidence on non-pharmacological management the committee made recommendations: • to support people with energy management • to support people with ME/CFS who feel ready to progress their physical activity beyond their current activities of daily living or would like to incorporate a physical activity or exercise into the management of their ME/CFS. • to offer CBT to help people manage their symptoms and to reduce the distress associated with having a chronic illness and are options for inclusion in the care and support plan where appropriate and chosen by the person with ME/CFS. To accompany this the committee have made recommendations that set out how CBT and strategies for energy management, physical activity and exercise should be delivered for people with ME/CFS. The symptom management section of the guideline includes advice on rest and sleep, physical functioning and mobility, orthostatic intolerance, managing pain, dietary management and strategies, and CBT. When considering the evidence for pharmacological interventions the committee agreed that there was insufficient evidence of benefit to recommend any medicines but recognised that people with ME/CFS have found some drugs helpful in managing the symptoms of ME/CFS and they could be discussed on an

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					individual basis and included recommendations on medicines for symptom management.(see Evidence reviews F,G and H) Throughout the guideline a holistic personalised collaborative approach to the assessment and the management of ME/CFS is recommended throughout the guideline and as part of this the management of symptoms should be fully explored with the person with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	034 - 036	General	There is no mention or recommendation about assessing mood in patients with ME/CFS. Making this assessment does not assume mood has played a part in aetiology, but it does have an impact on ongoing care and quality of life. This is true for any long-term condition and it should be explored, and we know there is a correlation of anxiety and depression in those with ME/CFS, though not causation. Neale FK, Christie D, Hargreaves DS*, et al* Illness duration, mood and symptom impact in adolescents with chronic fatigue syndrome/myalgic encephalomyelitis? *Archives of Disease in Childhood* 2020;105:911-912.	Thank you for your comment. After considering the range of stakeholders comments on the assessments in the guideline the committee have made the edits below and hope this add some clarification for the reader. In the assessment in the suspecting ME/CFS and assessment and care and support planning sections of the guideline, 'comprehensive clinical history' has been edited to 'medical assessment (including relevant symptoms and history, comorbidities, overall physical and mental health). In addition psychological wellbeing has been edited to, 'an assessment of the impact of symptoms on psychological and social wellbeing'. The review section of the guideline includes an assessment of a person's condition and an assessment of their psychological wellbeing. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. No differentiation is made on physical or mental health conditions. Also to note that after taking into consideration the stakeholder comments the committee have reviewed the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders to reflect the managing co-existing section of the guideline.

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University College London Hospital NHS Foundation	Guideline	021 - 022	001 - 022 001 - 012	Children and young people (CYP) are particularly sensitive (again, due to their neurodevelopmental age and stages) to being perceived as different, and many do not want wheelchairs or obvious aids. However, school buildings are often large with stairs and require an element of physical capability just to	Thank you for your comment and information. Further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion.

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Trust - TRACCS				navigate them. Some find aids like wheelchairs helpful in attaining education and independence. This should be decided flexibly individually on a patient-by-patient basis It should be noted that school is a place of activities beyond academic education and that the social element of attending school in person should not be dismissed. This is important to note, because of the statutory nature of education policy. A broad experience of enjoyable, social and learning activities should be the aim of CYP management; however a number of these activities can be achieved through the school experience. In our opinion, even if school makes things more difficult in some ways it should not necessarily be automatically reduced as it may take time to get used to the increased stimulation and stressors. Reduced timetables can help those who are not able to manage a full day or week to have the experience of being at school for some of each week.	
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	026 - 027	016 - 022 001 - 019	There appears to be a mismatch between physical activity and physical maintenance, which is achieved through a form of activity. Examples of what good physical maintenance might be across the different severity levels (rather than just passive stretching (as noted on pg 44) or going up and down stairs) may be helpful, as patients with mild ME/CFS may be able to walk to school or work etc. This should then be "maintained" during holidays in order that on returning they have not lost ability (deconditioned, not due to or as a cause of ME/CFS, but making restarting after holidays harder, and impacting on mood and ability).	Thank you for your comment. After considering the stakeholder comments the physical maintenance section has been renamed to 'physical functioning and mobility' and has been moved to the symptom management section of the guideline to provide clarity that it is about advice on maintaining and preventing the deterioration of physical functioning and mobility. After considering the range of stakeholder comments the committee agreed to remove the examples in the rationale recognising that approaches will be individual and in the context of the priorities and abilities that people may have.
University College	Guideline	027 - 028	020 - 024	The evidence for GET has been called into question, and reading Professor Jonathan Edwards and the evidence review,	Thank you for your comment.

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London Hospital NHS Foundation Trust - TRACCS			001 - 029	this can be understood. However, we have concerns that the evidence then used to make statements of harm is also of reduced quality as it is based on surveys conducted through special interests' groups where subjective bias of patient selection may be present. Is GET and CBT then not recommended because there is *possible* harm to patient and that is more important than possible benefit? If this is so, then we would ask how drugs can be recommended by NICE that may have side effects or harms. If this analogy is followed-through the one can see that there is difficulty here. As with medication, therapies (such as CBT and GET) need to be correctly prescribed and delivered in a way so that amounts are not harmful – and supervised appropriately. Patients should also be able to make informed choice about risk and be kept under review for either progress or harms. This is true evidence-based medicine. We are concerned that this guidance would prevent those who would achieve a benefit through activity may be denied that opportunity and may actually deteriorate. We felt that the previous 2007 guidance covered this well whilst it acknowledged the evidence quality was poor. In fact, it appears that on page 27-28 the guidance goes on to describe a physical activity programme very similar to GET, sharing the same principles of stabilising activity and then gradually increasing activity using flexible increments. . This is not a fixed automatic increment that a patient must carry out despite personal evidence of harm to self which is what is implied on page 28 line 6-7.	*Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *GET* Evidence reviews G and H describe the quantitative and the qualitative evidence for graded exercise therapy and includes the committee discussion The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people

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				It is therefore confusing to have an absolute statement of GET not being recommended, when this is followed by the type of exercise recommendations our team would practice as GET. Again we would ask, if this is about difficult terminology then could NICE ask for research into terminology that would be acceptable to patients and families. Language has an impact on perceptions of treatment, and therefore the subsequent outcomes.	with severe ME/CFS (Appendix 2). In summary, the clinical effectiveness evidence for GET was of low to very low quality and the committee was not confident about the effects. This when balanced with the mostly negative opinions about experiences of physical activity and GET reported in the qualitative evidence resulted in the committee concluding that GET should not be offered to people with ME/CFS. This conclusion remained the same after additional scrutiny of the populations included in the non-pharmacological evidence (See evidence review H appendices Fand G for the approach taken, the analysis and the impact on the results and interpretation of the evidence.) Based on the evidence mentioned above and their own experience the committee concluded that it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose this. The committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	055 - 056	028 001 - 003	We find it very concerning that the committee made recommendations around safeguarding based on their consensus, when acknowledging NO evidence exists in the area. This feels unsafe and beyond the scope of the committee and it should be reflected as to whether this was the most appropriate action to take.	Thank you for your comment. Safegaurding was discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.

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					Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	029 - 030	017 – 022 001 - 002	If the committee are making a number of recommendations relating to their experience and practice, then even when evidence is missing (such as for sleep management) it would still make sense that supplying information about sleep hygiene and techniques that have not been shown to be harmful would stand as a reasonable course of management. We also have experience of children and young people (CYP) who think they need energy drinks and caffeine when they have ME/CFS. Basic sleep education has led to improvement of sleep quality and quantity.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. The recommendations include that people should be given personalised sleep management advice.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	055 - 056	019 – 025 001 - 006	We think that these guidelines were lacking balance relating to safeguarding and would benefit from reminding professionals to remain professionally curious, not to lean too heavily on professional optimism and to hear the child's voice throughout their consultations (Munro 2011)[i], to ensure child visibility through interactions with professionals (Ferguson 2017)[ii] and that safeguarding should be considered as part of a differential diagnosis[iii] whilst considering some of the key recommendations from serious case reviews including the	Thank you for your comment. Safegaurding was discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families.

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				consideration of persistent non-attendance at appointments which could be part of a pattern of non-cooperation and indicate a risk of harm (Brandon et al 2010)[iv]. References: Munro, E (2011) Review Of Child Protection: Final Report - A Child-Centred System - Publications - GOV.UK. [online] Gov.uk. Available at: https://www.gov.uk/government/publications/munro-review-of-child-protection-final-report-a-child-centred-system {accessed 3rd December 2020} [ii] Ferguson, H (2017) How Children Become Invisible in Child Protection Work: Findings from Research into Day-to-Day Social Work Practice, The British Journal of Social Work, Volume 47, Issue 4, June 2017, Pages 1007–1023, https://doi.org/10.1093/bjsw/bcw065 {accessed 3rd December 2020} [iii] Child abuse and neglect NICE guideline [NG76] Published date: 09 October 2017 [iv] Brandon et al (2010) Building on the learning from serious case reviews: a two-year analysis of child protection database notifications DFE-RB040	Recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	005 - 006	027 – 029 001 - 006	Agreeing ways of communicating with the young person (YP) is important, as is understanding if YP require parents or carers or other aids to help communication. Thanks for flagging this. There also needs to be understanding that it is good practice to build in time to see the YP alone in order to explore symptoms & experiences they may be unable to share with their parent/carer. This is not an assumption of abuse – it is basic and essential paediatric care offered to every child and should	Thank you for your comment and information. The recommendation has been edited to reflect this. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme

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				be explored with each family. This guidance implies that children and young people (CYP) do not require the opportunity to have confidential conversations with professionals. We would recommend signposting to the HEEADSSS* psychosocial screening interview approach to conversations with CYP – where conversations around home, education, eating, activities, drugs/alcohol, sex, sleep, social media and safety are discussed with the young person as a screening tool for potential areas of risk and harm. * Doukrou M, Segal TY Fifteen-minute consultation: Communicating with young people—how to use HEEADSSS, a psychosocial interview for adolescents *Archives of Disease in Childhood - Education and Practice* 2018;103:15-19.	
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	005	023 - 026	This is a really important point about previous experiences. Thank you for adding this.	Thank you for your comment.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	006	007 - 029	It is important that people realise how severe ME/CFS can be, and so these sections are important. However, as these sections (on severe and very severe ME/CFS) form the main content throughout the guidance until the terminology is explained on page 41- we are concerned it will be overwhelming for children, young people (CYP) and their families who do not have symptoms to this extent and may be scared that this will happen to themselves or their child, thereby reducing hope.	Thank you for your comment. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These

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				We would suggest it would be very important and better to have definitions of mild, moderate and severe ME/CFS early on in the guidance to set a more balanced tone. This is especially important having reviewed the rationale and impact section (pg 47 onwards) where a number of "how this will change clinical practice" sections suggest that earlier diagnosis when a patient's symptoms are milder will prevent deterioration to severe ME/CFS and is used as justification for why it will not impact on resources. If this is the committees thinking, then perhaps more on mild/moderate ME/CFS would be helpful to encourage clinicians and patients to recognise these milder forms in themselves and patients and aid speed of diagnosis.	recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5). In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS. To provide clarity about the severity of ME/CFS and symptoms the definitions of severity have been moved from the terms used in the guideline to the front of the recommendations.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	007	004 - 016	Although the first part of the sentence reads "may mean that people:" the following bullet points actually all read as if these things will definitely happen to patients – again this is language that can be intimidating to those with milder forms and exclude those with mild/moderate forms as they don't think they fit the criteria for ME/CFS diagnosis.	Thank you for your comment. The bullet points follow from the stem of the recommendation,' recognise that the symptoms of severe or very severe ME/CFS may mean that people', indicating that these may happen and the group is identified as people with severe or very severe ME/CFS. Taking into account the range of stakeholder comments about the location in the guideline of this section the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section at the end of the guideline. In response to your comment this now means that the criteria for suspecting and diagnosing ME/CFS precedes this recommendation providing clarity about the symptoms that are related to a diagnosis of ME/CFS.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	007	001 - 003	Note about low stimulus environment. We have concerns that for some families this may result in a young person being limited to a dark room inappropriately and without their true consent. This points also covers choice around these decisions and for advocates, however this can be fraught and complex with children and young people and their parent/carers where the relationship is by its nature not one of equals, and parents unfortunately do not always act in the best interests of their child even when they wish to put their child first. We understand it is a delicate balance between unhelpfully assuming all parents are harming children and missing the few occasions where real harm is coming to the child or young person because the emphasis is put on Parent/carers advocating for their children without caveats of when and how to act around concerns (such as guidance on fabricated and fictitious illness) .	Thank you for your comment and information. Thank you for your comment. This section raises awareness about the symptoms that people with severe or very severe ME/CFS may have and how these may be managed. It is supported by Appendix 2,Evidence review C – access to care and the committee's experience. The committee agreed it was important to raise awareness about these symptoms and the support that may be needed to manage them, in this case hypersensitivity. The committee agreed that these recommendations could apply to children and young people with severe or very severe ME/CFS. The committee note that the level of support needed is individual to the person and agreed collaboratively as part of their personalised care and support plan with the health and social care professionals involved in their care. An assessment of benefits and harms would be part of this. The committee agree that issues around safeguarding are complex and this is addressed later in the guideline. In addition, after considering stakeholder comments on the principles of care for children and young people recommendation 1.1.6 has been edited to include, ' with or without their parents of carers as appropriate' to provide further clarity. The terms in the guideline section includes a definition of advocacy.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	007	022	Whilst it is important that HC professionals do not worsen the situation for patients, this may necessitate breaching confidentiality.	Thank you for your comment.
University College London	Guideline	008	005 - 009	For clinicians not providing specialist care in ME/CFS it may be more helpful to keep to the 2007 recommendations that helped support diagnosis and which investigations were helpful.	Thank you for your comment. Throughout the guideline the committee have recommended carrying out

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Hospital NHS Foundation Trust - TRACCS					investigations to exclude other diagnoses. The committee have now included examples of investigations that might be carried out. The examples are not intended to be an exhaustive list and the committee note that any decision to carry out investigations is not limited to this list. They emphasise the importance of using clinical judgment when deciding on additional investigations.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	009	002 - 023	These can all happen with ME/CFS but these are also symptoms of other significant and life-threatening illnesses that need further investigation before being attributed to ME/CFS. The point should be made more explicitly that even if a patient already has an ME/CFS diagnosis, they are not precluded from having other conditions and assumptions about what is attributable to the ME/CFS should not be made without due care, consideration and investigation. If a practitioner has any concerns regarding this, further referral should be made to specialist services.	Thank you for your comment. The committee agree and throughout the guideline the committee have recommended carrying out investigations to exclude or identify other diagnoses noting that when there is any doubt in interpreting signs and symptoms then advice should be sought from an appropriate specialist.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	010 024	017 - 019 014 - 015	The use of the term "energy envelope" rather than referring to baseline (which is mentioned later in the guidance) is felt to be restrictive. The image of an envelope is quite limiting whereas people can grow from a baseline. This creates the impression that it would be hard to increase energy capabilities and we feel it is not constructive for communicating with patients. We would recommend baseline.	Thank you for your comment. After considering the range of stakeholder comments the committee agreed that this concept and energy envelope might not always be appropriate when suspecting ME/CFS. They acknowledged that some people with suspected ME/CFS may not be diagnosed with ME/CFS and information on energy limits* may not be helpful. At such keeping a diary at this stage may not be appropriate. The committee amended the recommendation to advise people to manage their daily activity and not push through symptoms. *After taking into consideration the comments made by stakeholders about the potential for misunderstanding the committee agreed to edit energy envelope to use energy limits.
University College	Guideline	011	009 - 012	Despite multiple assertions in the rationale for recommendations section, there is no evidence presented by	Thank you. We acknowledge that there is not quantitative evidence that early diagnosis and intervention would have a

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London Hospital NHS Foundation Trust - TRACCS				this guidance that corroborates that early diagnosis and treatment does indeed reduce severity of ME/CFS and would therefore have a positive effect on resources. At this point in time, whilst this may be good practice, it is disingenuous to suggest it would not require an increase in resources. Indicating that all 4 sets of symptoms are required before diagnosis can be made is also helpful, but the likelihood is that when clinicians are unsure, they will use the 4-week symptom recommendation as a reason to refer if there is any confusion or uncertainty, and this would increase referral burden.	positive effect on resources. But conversely, there is not evidence that the proposed changes to the diagnostic process would increase resource use. The experience of the committee, which also reflects the experience of patients recorded in the qualitative evidence is that advice to exercise early in the course of their disease appeared to significantly deteriorate their symptoms. Therefore, the implication is that more appropriate management would improve outcomes. On that basis, one would expect some resource savings in the longer term, although not necessarily net cost savings overall. The rationale was already quite cautious but we have made it clearer by changing one sentence from "Earlier access to appropriate advice and care could prevent disease progression and therefore reduce resource use in the longer term" to "Earlier access to appropriate advice and care could prevent disease progression and therefore might lead to some resource savings in the longer term." This committee agree that this is good practice. The recommendation was to ensure that clinicians were alerted to the possibility of ME/CFS as soon as possible. Based on the qualitative evidence and their experience the committee agreed it is important that people with this combination of symptoms are given advice that may prevent them getting worse as early as possible. See Evidence review D- for the evidence and committee discussion. The committee discussion in Evidence review E-strategies pre diagnosis sets out the rationale for the committee's decision making for people with suspected ME/CFS. In reference to your comment they agree there is a lack of evidence on the advice to give people with suspected ME/CFS, but they agreed the advice

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					they have recommended in section 1.3 would not be harmful in the short term. In addition committee note that it is important to consider that people that are suspected of ME/CFS but not diagnosed with ME/CFS may follow this advice and it would not cause harm to anyone. After considering the stakeholder comments the committee agreed to make some edits to the recommendations on suspecting and diagnosing ME/CFS and hope this has addressed some of your points and added some clarity for readers. In summary the edits to the points you make are: • 'Provisional' diagnosis has been deleted for the following reasons: o The committee agreed the term 'provisional diagnosis' was confusing while waiting for the results of any assessments to exclude other conditions before diagnosis at 3 months. This section now focus solely on suspecting ME/CFS. Diagnosis is now introduced at 3 months. o The risks of early diagnostic labelling, the committee agreed that people with suspected ME/CFS could be give advice without the need to be told they have a provisional diagnosis
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	012	010	Management plan - this is an important element of good quality equitable care.	Thank you for your comment. Management plan has been edited to 'care and support plan' in line with personalised care and support plans https://www.england.nhs.uk/ourwork/patient-participation/patient-centred/planning/.)

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	014	019 - 021	This statement is unhelpful as "less common to have long periods of remission" has little meaning with two unqualified statements of time and probability.	Thank you for your comment. After considering the range of stakeholder comments the committee have edited this bullet point and hope this addresses your point: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	015	012 - 015	We feel that this paragraph would benefit from adding that social care also provides a statutory safeguarding response, whereby engagement is not voluntary, and families might not experience this as helpful.	Thank you for your comment. This section is about the support people with ME/CFS can access. Safeguarding is addressed further in the safeguarding section of the guideline.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	015	001 - 003	The TRACCS team has significant concerns about this section. The tone set by page 14 lines 19-24 is one of a life -long debilitating illness which people are unlikely to significantly recover from. Whilst we are pleased that the guidance separates out children and young people (CYP) as having improved outcomes, we are concerned that "the outlook is usually better" does little to assuage that negative tone because better than a small proportion still appears small. As the prognosis section starts with "people" rather than adults – CYP and their parents may not get to the part about their better outcomes and may just read this bit. We would recommend that even if figures are highly variable, putting some numbers in the guidance to direct conversation is more helpful than vague terms. These could of course be caveated with "the numbers are mixed, but it would appear that x% improve, x% stay the same, and x% can have significant difficulties for many years."	Thank you for your comment and information. After considering the range of stakeholder comments the committee have edited these bullet points and hope this addresses your points: • varies in long-term outlook from person to person – although a proportion of people recover or have a long period of remission, many will need to adapt to living with ME/CFS • varies widely in its impact on people's lives, and can affect their including their daily activities, family and social life, and work or education, (these impacts maybe severe) • usually has been removed from recommendation 1.6.5 . Carruthers (2011) has been included in evidence review D. We note the statement about higher rates of recovery is vague.

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				We understand that the following papers show evidence of CYP recovery that is better than in adults. - Carruthers BM, Van de Sande MI, De Meirleir KL et al (2011) Myalgic encephalomyelitis: international consensus criteria. Journal of Internal Medicine 270: 327-338. 'Children and young people with CFS have a significantly higher rate of recovery when compared with adults' - Crawley, E (2017): The reported recovery in young people is between 54 and 94% - Crawley E (2017) Paediatric chronic fatigue syndrome: current perspectives: Paediatric Health Medical therapy, 9:27-33 - Rowe (2019) Young people have a mean duration of CFS for 5 years, with 68% reporting recovery by 10 years (Rowe KS (2019) Long term follow up of young people with chronic fatigue syndrome attending a paediatric outpatient services. Front Paediatrics 7:21) None of these papers appear to be reviewed in evidence section A or evidence section B which are the ones recommended to read at the end of this section. These figures would suggest that over 50% improve, which is more than a small proportion. We would ask the committee to use these references additionally to inform the prognosis section and additionally advise ask for more research into this, specifically in CYP.	Crawley (2017) is literature review so did not meet protocols for any of the review questions. Rowe (2019) had an observational study design including questionnaire with closed questions and open questions (no thematic analysis) and did not meet protocols. The statement about recovery was based on self-reports. The committee has considered the potential for better outcomes and greater chances of recovery in children and young people. This has been acknowledged in the guideline but, considering the variability of ME/CFS from person to person and of its impact on peoples' lives, the committee also agreed it would not be appropriate to include specific figures to convey this.
University College London Hospital NHS	Guideline	015	008	When applying this to children and young people (CYP) who are likely to improve over time, it would be important to prepare families for the potential *loss* of benefits that may result.	Thank you for your comment. This section is about to support people in accessing benefits, the withdrawal of benefits is not relevant here.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	016	006 - 011	We were concerned that having the sentence on point 7 & 8 which states "should be carried out or overseen by health and social care professionals who have training and experience in ME/CFS" is not realistic as safeguarding assessments can appropriately be carried out by professionals who do not have specific expertise in this area, but we agree that an awareness of chronic illnesses and how these can affect and impact children and young people and their carers is important. We would like some reconsideration of the wording on point 10 & 11. We think it would be helpful to add that some of these symptoms may be indicators of abuse and that the symptoms shouldn't stop professionals from exercising their professional curiosity about these symptoms or from following their usual safeguarding protocols if they are worried that a child is at risk of significant harm.	Thank you for your comment. The committee agreed that all staff delivering care to people with ME/CFS should have training relevant to their role so they can provide care in line with the guideline and this is included in the recommendations in the training for health and social care professionals section of the guideline. With regard to Safegaurding the importance of this is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. *Point 10 and 11* The wording of the recommendation is, 'the following are not necessarily…' this does not indicate that they are never signs of abuse or neglect. The following recommendation is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The NICE guidelines on child maltreatment and child abuse and neglect should be followed. This is clear that if a professional has concerns they should be addressed in the same way as with any child or young person. This is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	016	012 - 015	We can understand the importance of having safeguarding professionals with an understanding of ME/CFS. However, the resources required to have emergency assessments within 24 hours by professionals who have training and experience in ME/CFS has not been noted and instead no further resources are felt to be required.	Thank you for your comment. After considering the stakeholder comments the reference to 24 hours has been removed to acknowledge the involvement of health and social care professionals with ME/CFS may be later in the process.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	017	008 - 010 011 - 019	Indeed these are not necessarily signs of abuse or neglect. However, we feel the way this is phrased in the guidance may undermine professionals with reasonable concerns about safeguarding issues and that professional curiosity and sensitive exploration should be encouraged. It is paramount that the needs and wellbeing of the child are placed central in this part of the guidance. As such, we think that point 8 should be re-worded as "recognise that the following may or may not be indicators of signs of abuse or neglect….." There needs to be very clear exploration and transparency around the reasoning regarding a young person declining or withdrawing from any part of a management plan, especially for younger children by their parents or carer, as perhaps would be the case for any child whose parents are making treatment decisions that are not viewed in the best interest of the child. We think that this paragraph would warrant a link to the Fabricated and Induced Illness guidelines[2] in order for practitioners to consider if this is a concern. Reference:	Thank you for your comment. The importance of this section is discussed at length in the committee discussion in Evidence review B. In summary the committee discussed how a lack of knowledge and understanding about ME/CFS and the nature of the symptoms has led to people not being believed and this has had negative consequences particularly for children and young people, and their families. The following recommendation 1.7.5 is clear that recognising and responding to possible child abuse and neglect (maltreatment) is complex and should be considered in the same way for children and young people with confirmed or suspected ME/CFS as with any child with a chronic illness or disability. The principle applies to adults. This is clear that if a professional has concerns they should be addressed in the same way as with any person. Recognising that this can be compounded by the risk of symptoms being misunderstood is the reason the committee have recommended that health and social care professionals who have training and experience in ME/CFS should be involved to support this process and identify where there might be a risk.

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				Department of Children schools and families (2008) Safeguarding children in whom illness is fabricated or induced Supplementary guidance to Working Together to Safeguard Children DCSF-00277-2008	
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	018	010	We are concerned about the phrase "do not discharge". We thought this would benefit from rewording such as "Thoughtful consideration should be given to someone who misses appointments because their symptoms have worsened. Contact them to explore why they could not attend, how to support them and consider, if they are children or young people, whether there are concerns around parental ability or capacity which may hinder a person with ME/CFS to access health and medical treatment. Worries should be escalated via the usual safeguarding protocols if needed".	Thank you for your comment. After considering the stakeholder comments the committee edited this recommendation to, 'If a person with ME/CFS misses an appointment: • do not discharge them for not attending because it could be due to their symptoms worsening • discuss why they could not attend and how the multidisciplinary team can support them' and hope this addresses your points. Safegaurding is addressed in section 1.7 of the guideline.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	020	020 - 021	In our teams' experience the wait list for aid and additional resources can be up to a year. Whilst we support the need for adaptations to improve a patients' quality of life this statement may create unrealistic expectations that result in a difficult relationship with social care and OT. Funding for home adaptation (disability facilities grants- DFG) is for those with permanent or long-term disability- so if the mean duration for young people with ME/CFS is 5 years (Rowe, 2019), then this is not a suitable suggestion of allocation of resources (and will not meet most local authority criteria), and thus home adaptations are likely not suitable for children and young people and this should be outlined in the guidelines (Rowe KS (2019) Long term follow up of young people with chronic fatigue syndrome attending a paediatric outpatient service. Front Paediatrics 7:21)	Thank you for your comment. After considering the stakeholder comments the committee added, 'provide access to aids and adaptions' to add clarification that this is about signposting to support.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	020	016	We think that it is important to add "Parental ability to support children and young people to access appointments and to support the young person to be seen alone by the professional if age and developmentally appropriate".	Thank you for your comment. After considering the stakeholder comments the committee have added that the points listed are a minimum, taking into account that an assessment should be personalised and for this reason no other examples have been added.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	021	006 - 010	Again, the tone of this bullet point is negative. It may be more encompassing to express it as "people have variable responses when returning to work, school or college and therefore this requires planning and consideration as hours are increased with reasonable adjustments being applied to prevent worsening of symptoms. Specialist support from people experienced in helping advocate and navigate returning is recommended." More positive presentation of information regarding flexible ways to access school can reduce fear and anxiety around changes, which in itself may be prohibitive and unhelpful. Line 8-10 – there could be more clarification as to what adjustments could be. UCLH TRACCS service would be happy to help with providing clarification. There are also risks to *not* returning to school, education or work and this should also be considered.	Thank you for your comment. After considering the range of stakeholder comments the recommendations in this section have been reordered starting with accessing support. Recommendation 1.9.4 provides specific information on children and young people. Further information on the school environment is included in Evidence review A-Information for people with ME/CFS and the points your raise are highlighted in the committee discussion.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	024	021 - 024	Having a flexible approach is essential to management of ME/CFS. However, it should be noted that (as the guidance says) there can be a fluctuation in symptoms through days, weeks and months and that therefore an overall aim to increase and improve activity level is helpful. It is likely to be confusing, and potentially impact rapport with professional therapists, if patients think they can never make any increments when	Thank you for your comment. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is

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				feeling slightly worse (as implied by this section), when overall this may be appropriate with guidance and support. The fear of increasing exercise and activity that may arise after reading this guidance could prevent progress in patients who may have improved. Good quality education around the condition for patients & development of relationships are key here.	never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies).
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	024	004 - 005	"No current treatment" is misleading as later discussion about energy envelope, baselines and activity management and physical maintenance can appear confusing as what are these techniques if not a form of treatment? Perhaps the committee's definition of treatment should be outlined in the "terms used in this guidance section"	*Thank you for your comment.* *Cure or treatment* After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' in the recommendations where it is alongside 'cure' to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	025	018	Patients may not need to automatically reduce activity as a first step, they may need to make adjustments to how, when and what activity they do to create a more even approach consistent with pacing. It would be helpful to mention the use of an activity diary as a first step so that overall activity levels can be analysed before decisions regarding adjustments are made.	Thank you for your comment. After considering the range of stakeholder comments this was edited to, 'agree a sustainable level of activity as the first step, which may mean reducing activity'.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	027	024	Having a list of "Do Not offer" early in the guidance for physical activity presents activity as a potentially dangerous pursuit, and we feel that a fearful tone may not be helpful to patients. We would firstly think that putting any "Do Not offer" *after* positive approaches to physical activity would be helpful, and secondly suggest that perhaps "Careful thought should be given to the appropriateness of activity that is based on: …." May be a better start.	Thank you for your comment. Based on the evidence* and their own experience the committee concluded there are clear indications about what type of physical activity or exercise programmes should not be offered to people with ME/CFS but it was important that a physical activity or exercise programme is available for people with ME/CFS where appropriate and where they choose to explore this. The

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				The issue with "Do Not Offer" is that this didactic approach to treatments (including osteopathy) that patients may have found helpful, and for which known harms are not clear could alienate patients who have found it helpful. If the evidence is low quality then Do Not Offer appears unnecessarily contentious. The later emphasis on individualised care is important to avoid any harms to patients. We are concerned that the guidance presents activity and exercise in a negative light, without acknowledging to what degree many patients want to get back to high functioning activity (like running or cycling etc) that were an important part of their lives and wellbeing previously. Public Health England recommends exercise because it is associated with lower mortality and this should not be dismissed, instead the difficulties for patients with ME/CFS should be acknowledged. Ways to do gentle and manageable exercise should be explored as well as the uncertainty this can cause about what helps one be well, and what contributes to one being unwell. We agree that highlighting individualised plans around increased activity and exercise are essential and in this way specialised therapy is important. However, the tone towards exercise generally should be more positive.	committee recognised there are people with ME/CFS that may feel ready to incorporate a physical activity or exercise programme into managing their ME/CFS and want to explore this option. Where this is the case the committee agreed that it was important that they are referred to and supported by physiotherapists and occupational therapists that are trained and specialise in ME/CFS to do this safely. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care. *See Evidence reviews G and H, these describe the quantitative and the qualitative evidence for physical activity and exercise interventions and includes the committee discussion. The committee discussed this evidence with the findings from the review on access to care (report C), diagnosis (report D), multidisciplinary care (report I) and the reports on Children and Young people (Appendix 1) and people with severe ME/CFS (Appendix 2). After considering the stakeholder comments, physical activity or exercise has been added to aid clarity in the recommendations in this section. *Lightning Process, osteopathy, life coaching and neurolinguistic programming* After considering the stakeholder comments the committee agreed to edit this recommendation to,' do not offer the Lightning Process or therapies based on it to people with ME/CFS'. The committee agreed that concerns raised in the qualitative evidence about the Lightning Process could not be ignored and

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					that it was appropriate to have a do not recommendation. (See evidence reviews G and H)
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	028	023 - 029	This is what would be expected of a specialist physiotherapist in this field as recommended in 16-18.	Thank you for your comment.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	028	012 - 015	We agree that physical activity should be discussed in line with patient wishes. This should be explored regularly with balanced conversations around risk of both engaging and not engaging in increased activity to ensure informed decision making.	Thank you for your comment.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	028	019 - 022	Putting the most negative outcome first does not read correctly. It creates an impression of overall negativity without evidence to back this up. Whilst making note of negative outcomes is important, the problem with the tone leaning towards negativity is not purely one of difficulty in reading. It has an impact on the relationship the patient has with their illness and their management and the nocebo effect (expectation of a negative outcome results in a more negative outcome compared to baseline) is also well known and powerful.	**Thank you for your comment.** When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience while acknowledging the substantial incapacity that some people have as a result of ME/CFS. After taking into consideration the comments from stakeholders about the negative tone of the guideline the committee reviewed all the recommendations and edited those they agreed had a negative tone. These recommendations now better reflect all people with ME/CFS (for example, recommendation 1.1.1) and the long term outlook (see recommendation 1.6.4) with particular reference to children and young people (see recommendation 1.6.5.).

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					In addition, the committee have revised the structure of the guideline highlighting the special considerations of people with severe and very severe ME/CFS in an individual section. The committee agreed this would ensure that the particular needs of people with severe and very severe ME/CFS were not hidden within the guideline nor mistaken to reflect the experience of all people with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	028	016 - 018	This will require additional resources.	Thank you for your comment. The guideline reflects the evidence for best practice. There are areas that may need support and investment, such as access to ME/CFS specialist services, to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed. Your comments will also be considered by NICE where relevant support activity is being planned.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	028	025 - 027	The establishment of baseline is important part of therapy. However, it does not then follow that this automatically requires a reduction in activity. What may be required is a flattening of the boom and bust periods. It should also be noted that some activity that the patient is engaging in may be maintaining mood and preventing anxiety. If this is automatically withdrawn the impact could be significant, especially in children and young people (CYP).	Thank you for your comment. This is to ensure the person starts the programme at a level that does not worsen symptoms and to ensure this level is maintained until flexible adjustment are agreed. As you note this is a personalised physical activity or exercise programme and would be agreed with the person and reviewed regularly.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	029	017 - 022	It is not clear why excluding the recommendation in the 2007 guidance around explaining the impact of sleep on patient symptoms has been removed.	Thank you for your comment. After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people

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					should be given advice on the role of rest and sleep and personalised sleep management advice.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	029	017	This section does not include anything about sleep. If as per the rationale section this is because there is no good quality evidence for sleep management then this should either be excluded from the guidance or explicitly noted in the recommendations. However, as far as we are aware, there are excellent sleep resources from specialist clinics such as at the Evelina, and many specialist services use materials to aid improving quality of sleep.	After considering the stakeholder comments the committee agreed to include consensus recommendations on sleep management for people with ME/CFS. There was a lack of evidence identified for rest and sleep strategies and the committee were unable to give specific advice about strategies recognising the approaches should be tailored to the individual. The recommendations include that people should be given advice on the role of rest and sleep and personalised sleep management advice.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	033	023	We would advise care around the recommendation of enteral feeding without thorough investigation and specialist review of its appropriateness and what this would entail. We would recommend specialist dietetics and gastroenterology input from someone with experience in this area.	Thank you for your comment. The committee agree and the first recommendation in this section is to refer people with severe or very severe ME/CFS for a dietetic assessment by a dietitian who specialises in ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	034	012 - 030	Again, by starting with the most negative point, the whole tone around CBT changes. It would be more customary for this to be the last point (is not curative). It is not treatment and it is not cure, followed by a list of reason why it might be helpful is confusing. Again, we would ask the committee to consider what it means by the term treatment. We note the NICE guidance for T1 diabetes mellitus recommends psychological support for children and young people if they need it, acknowledging the impact of living with a chronic condition. This would be a good model for the committee to consider.	Thank you for your comment. After considering the range of stakeholder comments this has been edited , 'explain to people with ME/CFS that cognitive behavioural therapy (CBT) may help them to manage their symptoms but it is not curative'. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.

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					CBT is not a treatment for ME/CFS but could be useful for some people with ME/CFS with supporting them in managing their symptoms.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	034	006 - 008	The offer of CBT by professionals with experience of ME/CFS appears to directly contradict the expert testimony given by Jonathan Edwards where he was concerned that professionals expert in ME/CFS CBT were basing their therapy on unsound aetiology of ME/CFS and potentially doing harm. If this is a concern of the committee then further clarification is needed as to what they mean by someone who has expertise in CBT for ME/CFS.	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee

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					concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations).
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	036	012 - 021	Symptoms and signs of depression and mood disorder can also present as similar to ME/CFS symptoms and this should be considered not only as a possible co-morbidity, but as the underlying diagnosis.	Thank you for your comment. Throughout the guideline the committee have reinforced the importance of excluding or identifying other conditions and seeking advice from an appropriate specialist if there is uncertainty about interpreting signs and symptoms. No differentiation is made on physical or mental health conditions. Also to note that after taking into consideration the stakeholder comments the committee have reviewed the list of differential diagnosis in Evidence review D and added, mental health conditions: anxiety, depression or mood disorders to reflect the managing co-existing section of the guideline.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	036	005 - 011	Does this mean that all patients should be investigated for thyroid disease and coeliac as this is the implication for this section? If so, this should be explicitly stated, rather than potentially missing important investigations. By singling out these two conditions it appear that these are known relatives of ME/CFS or the most likely multimorbid conditions. However the rationale for recommendations makes no note of this, and leaves the reader confused and unsure about investigating other possible conditions, or associations. This relates to the diagnosis section where the previous list of investigations has been removed.	Thank you for your comment. Investigations Throughout the guideline the committee have recommended the importance of carrying out investigations to exclude other diagnoses. After considering the stakeholder comments the committee have now included examples of investigations that might be carried out. The managing co-existing section of the guideline includes links to NICE guidance where there is related guidance. It does not

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					infer any importance of the condition in reference to co-existing with ME/CFS. After considering the stakeholder comments the committee removed the reference to the NICE guideline on Coeliac disease and added the NICE guideline on irritable bowel syndrome in adults..
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	044	012	This recommendation has caused concern in our team as Prabu RKR, Swaminathan & Harvey LA (2013) (Passive movements for the treatment and prevention of contractures. Cochrane Database of Systemic Reviews.) have shown that passive movements do not prevent contractures. Instead our team advocate for 24-hour positioning, with each stretch of a muscle group lasting at least 8 hours. Active movement is important here, and this should be openly discussed with patients to balance reducing risk of significant consequences (contractures, pressure sores, DVTs etc) versus exacerbation of ME/CFS symptoms.	Thank you for your comment and information. The reference to contractures has been removed from the definition of physical maintenance. To note the physical maintenance section has been renamed to physical functioning and mobility.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	045 046 047	021 – 026 All 001 - 006	Recommendations for research - Prof Jonathan Edwards, UCL has expressed extensively his concerns regarding the clinical trial designs for therapy treatment for ME/CFS , particularly regarding bias, lack of blinding and subjective outcomes (Expert testimonies section Appendix 3 p6-13). Pg 46 line 1-3: Whilst this seems to refer to Jonathan Edwards points about the quality of data from non-blinded subjective trial outcomes, this is not explicitly stated, nor is there a recommendation for reviewing novel types of research around this area which was minutely examined and found wanting by Professor Edwards (with some reason). If NICE were to make a more visible statement to this fact in this guidance it would	Thank you for your comment. Design of trials The committee have made a research recommendation for the development of a core outcome set to improve the implementation of research in ME/CFS. The committee have included in the research recommendations on interventions the importance of long term follow-up. All NICE research recommendations are reviewed by the NIHR to consider for their funding streams. Other research funders also consider NICE research recommendations. It is beyond the remit of the guideline to provide more detailed information on how research in these areas should be conducted.

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				help push forward this type of research and avoid future concerns and confusion	
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	048	009 - 013 + 022 - 024	With regard to this paragraph, and earlier paragraph about not discharging patients that are unable to attend care there would be resource implications. Whilst specialist input is important in ME/CFS, if families and patients are not engaging with the care offered, then teams would be required to keep a number of patients as part of their service which are not receiving specialist input, and thereby would reduce the possibilities for another patient to benefit from this. Whilst it is important patients are not discriminated against for declining treatments they are within their rights to do so, it should also be important for professionals to engage with families as to why this is, and what the service can realistically offer them.	Thank you for your comment. The committee discussed discharge from services and agreed that any decision was a collaborative decision and there are not any set rules for how long someone should be in services with no one single model of care. Some of the committee members described experience of 'revolving door' services, when people with ME/CFS could contact specialised services when they required support.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	059	010 - 019	We would like to suggest that the assertion that specialist MDT teams would improve care and so in the end the patients would be better (and subsequently there would be an even or no need for further resources) requires elaboration & thought. The guidance sets a very negative tone for outcomes and says there are no treatments or cures for ME/CFS, and yet recommendations for specialist care throughout the guidance are noted alongside the supposition that patient outcomes will improve and therefore services will not be further burdened. This appears contradictory. If the committee do not think this is contradictory, then we would suggest that one of the research recommendations be for clearer idea of outcomes /outcome measures(not just what they should be) in ME/CFS and what would be considered enough of an improvement to be discharged from a service. (i.e. be considered a 'successful" treatment under specialist care.	Thank you for your comment. To note after considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS. The committee have reinforced the importance of ME/CFS specialist services throughout the guideline and where access to these services is required. They have recommended that parts of the care and support plan should only be delivered or overseen by healthcare professionals who are part of a ME/CFS specialist team, for example, for confirmation of diagnosis, development of the care and support plan, advice on energy management, physical activity, and dietary strategies.

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University College London Hospital NHS Foundation Trust - TRACCS	Guideline	062	001 - 006	This recommendation requires specialist occupational therapy and physiotherapy , of which there is already a shortage nationally. The hopeful end sentence that if people improve or maintain their health this will be highly cost effective may be correct, but we would question if it is realistic compared to the tone of the rest of the document where poor outcomes, no treatment and no cure is emphasised throughout. How then can specialist input make a difference, if no treatment is actually known to improve outcomes.	Thank you for your comment.. Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that all people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. (see evidence review G- self management strategies) In addition based on the quantitative and qualitative evidence (evidence reviews A, F,G and H and their own experience the committee concluded that it was important that a physical activity or exercise programme is considered for people with ME/CFS where appropriate and where they choose this. When developing the guideline the committee was mindful of the importance of developing a guideline for all people with ME/CFS. Throughout the process the committee recognised the difficulty in finding the balance to reflect the variation in the impact and severity of symptoms that people with ME/CFS experience. The committee acknowledged there are people with ME/CFS that may choose to incorporate a physical activity or exercise programme into managing their ME/CFS. Where this is the case the committee agreed that it was important that they are supported by healthcare professionals that are trained and specialise in working with people with ME/CFS. See evidence reviews F and G, where the committee outline where it is important that professionals trained in ME/CFS deliver specific areas of care.

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					After considering the stakeholder comments on the wording 'treatment or cure for ME/CFS' the committee agreed to remove the word 'treatment' from these recommendations to avoid any misinterpretation with the availability of treatments for the symptom management for people with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	065	008 - 022	It would be helpful to make a note of the impact of pain and nausea on patients (as done in the orthostatic section) because the impression from this guidance is that it is incidental compared to other symptoms, which is contradictory to our experience.	Thank you for your comment. A link to the suspecting ME/CFS section has been added to the committee's rationale for managing pain. This has not been added to the rationale for nausea recommendation as the experience of nausea can be related to many symptoms that people with ME/CFS experience. The committee disagree that nausea is incidental compared to other symptoms and experienced by many people with ME/CFS.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	065	021 - 022	If recommendations are based on experience of the committee then this should be stated explicitly.	Thank you for your comment. This paragraph states that there was an absence of evidence and the committee made a consensus recommendation.
University College London Hospital NHS Foundation Trust - TRACCS	Guideline	070	010 - - 012	We agree that the involvement of a paediatrician is important in children and young people (CYP) with ME/CFS.	Thank you for your comment.
University College London Hospital NHS	Guideline	071	General	There is a change in name from CFS/ME to ME/CFS but the explanation why is confused. If there is no evidence of brain inflammation we would suggest that NICE could propose research into a term that both patients and professionals were	Thank you for your comment. The committee agree that none of the currently available terms are entirely satisfactory. The rationale for using ME/CFS was

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Foundation Trust - TRACCS				happy with (there was some note of the American guidance). We agree this discussion is really important as confusion over terminology can cause difficulties with communication and rapport when seeing patients. We would appreciate NICE using its position to make a clear recommendation with regard to this to prevent discussions around terminology getting in the way of good quality care for patients.	initially set out in the scope for the guideline, *'This guideline scope uses 'ME/CFS' but this is not intended to endorse a particular definition of this illness, which has been described using many different names*'. The context section notes that *Many people with ME/CFS consider the name 'chronic fatigue syndrome' too broad, simplistic and judgemental'.*
University College London Hospital NHS Foundation Trust - TRACCS	Question from comments form	1		1: Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. Currently the following recommendations would most impact practice: - Referral to children's services after 4 weeks of symptoms for specialist medical team as referrals will increase with some diagnoses of post viral fatigue in this time frame. - Referral to specialist OT and physiotherapist will require an increase in budget and increased numbers of trained staff as specialist input is required for management - Referral to social care for review of aid and supports - resulting in increase in referral with no increase in resources. - The recommendation that appointments are adjusted in time, place, frequency including home visits as the patient requires will require increase in all staff (medical, OT, Physio, psychology, safeguarding) to be able to be flexible to this extent and travel from the hospital to patient homes. As a tertiary service that works nationally – this would also limit what we could	Thank you for your comment and information. The guideline reflects the evidence for best practice. The committee agree that there is variation in the delivery of some of the recommended services across the NHS. There are areas that may need support and investment, such as more flexible access to care , to implement some recommendations in the guideline. However, this guideline highlights areas where resources should be focussed and those interventions that should not be recommended, saving resource in other areas. Your comments will also be considered by NICE where relevant support activity is being planned.

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				practically offer and may therefore reduce the accessibility if we had to change the geographical area we covered in order to facilitate home visits. All of these changes would increase the amount of work expected of the service and have implications for staff, patients, costs etc. Our service is run on a block contract currently.	
University College London Hospital NHS Foundation Trust - TRACCS	Question from comments form	2 18 72	40 20	2 Would implementation of any of the draft recommendations have significant cost implications? We are concerned about references to not needing any additional resources to deliver care - there would be resource implications in: • providing training to other services to get them to a level of specialist; (line 18, p40) • Re-training or re-designing training with new, previously unused terminology • Home visits • meeting the "access to care" guidance • providing key-working roles, • in fulfilling what will be an extended role with Social Services re assessing for aids and adaptations (line 20, p72), • meeting the increased need for specialist occupational therapists (OT) , dieticians, and physiotherapists (PT) outlined in guidance as only OT/PT can provide some of the input. • Single rooms are not always available, There is the initial need for these changes in practice with cost implications of setting up, training and adding new members to the team and maintaining costs.	Thank you for your comment. The committee agree that flexibility in accessing services is important to all people with ME/CFS as the symptoms experienced can mean physically attending appointments can be difficult particularly for people with severe or very severe ME/CFS. In the Access to care section of the guideline and section on people with severe and very severe ME/CFS home visits are used as examples of supporting people with ME/CFS to access care. The committee note that other methods, such as online communications may be more appropriate depending on the person's symptoms. The NICE implementation team are assessing the resource impact of recommendations. We acknowledge that there is likely to be an increase in specialist resources required in some parts of the country in order to make the provision of care more equitable than it has been in the past. Commissioners will decide how best to implement this locally. We note that the recommendations do not emphasise continued involvement by the specialist team. Instead, the focus is on an initial assessment and management plan by the team. Follow up should continue to take place by the general primary care team.

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University College London Hospital NHS Foundation Trust - TRACCS	Question from comments form	3		3 What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) - Resource information packs - Examples of good practice in TRACCS: clear pathway; patient information leaflets - Examples of the suggested management plans, who would have access to them, and what areas should be covered would be helpful	Thank you for your response. We will pass this information to our resource endorsement team. More information on endorsement can be found here https://www.nice.org.uk/process/pmg29/chapter/the-nice-endorsement-programme. NICE routinely produce baseline assessment and resource impact tools. To encourage the development of other practical support tools, we run an endorsement scheme aimed at encouraging our partners to develop these in alignment with NICE recommendations. Eligible tools are assessed and if successful, will be endorsed by NICE and featured on the NICE website alongside the relevant guideline.'
VIRAS	Guideline	General	General	VIRAS group members are qualified in science and research and include healthcare professionals from various disciplines as well as carers for and patients with M.E. and Lyme disease. We were stakeholders for the NICE guidelines for Lyme disease and we welcome the opportunity to provide our comments on the draft guideline for M.E. The suggestions provided below could result in considerable cost savings while improving patient care.	Thank you for your comments.
VIRAS	Guideline	General	General	Medical professionals have been exposed to misinformation about M.E. and CFS for at least 13 years since the publication of the 2007 NICE guideline which promoted CBT and GET as treatments for the illnesses. Intentionally or otherwise, the guideline gave credence to the theories underlying these 'treatments', that the diseases are caused or perpetuated by 'fear avoidance behaviour' and 'deconditioning'. Although the draft is a great improvement, it would be wishful thinking to believe that the new guideline will eliminate the stigma associated with the diseases or put an end to harms resulting from the theories behind using CBT and GET as treatments. The	Thank you for your comments and information.

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				publication of the PACE Trial in 2011 was accompanied by fanfares in national newspapers and other worldwide media, falsely claiming that with either GET or CBT, 60% improved and 30% recovered. The deluge of misinformation appeared to confirm NICE's decision to include therapies that effectively branded patients as lazy, hypochondriac and neurotic. E.g., media headlines pronounced: The Daily Mail: Got ME? Fatigued patients who go out and exercise have best hope of recovery, finds study The Independent: Got ME? Just get out and exercise, say scientists The Guardian: Study finds therapy and exercise best for ME The Telegraph: Exercise and therapy can help ME sufferers, study claims The Daily Express: TRIAL OFFERS HOPE FOR ME SUFFERERS The Daily Record: Exercise and therapy can reverse effects of ME The Daily Star: TRIAL OFFERS HOPE FOR ME SUFFERERS Reuters: Pushing limits can help chronic fatigue patients (Please see: http://www.scribd.com/doc/112487732/Media-Coverage-of-the-PACE-Trial for links to online originals and complete articles.) The media reports repeated false and misleading claims for the efficacy of CBT and GET: REUTERS • Helping chronic fatigue syndrome patients to push their limits and try to overcome the condition produces a better rate of recovery… • The results showed that CBT and GET benefited up to 60 percent of patients, and around 30 percent of patients in each	

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				of these treatment groups said their energy levels and ability to function returned to near normal levels. DAILY EXPRESS • ME sufferers have been offered new hope following a landmark study which suggests the condition can be reversed with counselling and exercise. • The ground-breaking study is the most comprehensive to date and challenges the widely accepted belief that the illness cannot be cured. • Researchers found six in 10 patients reported significant improvements after undergoing either cognitive behavioural therapy (CBT) - a type of counselling which helps people take charge of issues, while encouraging them to increase their activity - or graded exercise therapy (GET), which is based on gradually increasing exercise. • Half of these people reported a return to "normal" energy levels. BBC • With cognitive behavioural therapy, 30% of patients returned to normal levels of fatigue and physical function. DAILY MAIL • It may seem counter-intuitive to patients suffering with fatigue, but scientists have found encouraging people with ME to push themselves to their limits gives the best hope of recovery. • The results showed that CBT and GET benefited up to 60 per cent of patients, and around 30 per cent of patients in each of these treatment groups said their energy levels and ability to function and returned to near normal levels. SCOTSMAN	

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				• ME SUFFERERS have been offered hope following a study which suggests the condition can be reversed with counselling and exercise. • The study is the most comprehensive to date and challenges the belief that the illness cannot be cured. • Researchers found six in 10 patients reported significant improvements after undergoing either cognitive behavioural therapy (CBT) - counselling which helps people take charge of issues, while encouraging them to increase their activity - or graded exercise therapy (GET), which is based on gradually increasing exercise. • Half of these people reported a return to "normal" energy levels. THE INDEPENDENT • The best therapies are those which help patients test the limits of their capacity, such as by gradually increasing the amount of exercise they take, the research shows. • Overall, 60 per cent of patients who received CBT or GET made progress and 30 per cent recovered sufficiently to resume normal lives. THE GUARDIAN • Chronic fatigue syndrome study finds more people recover if they are helped to try to do more than they think they can… • It found that patients showed more improvement – and a small minority recovered completely – after cognitive behaviour therapy (CBT) DAILY RECORD • CHRONIC fatigue syndrome can be reversed with counselling and exercise, a new study claims.	

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				- Six in 10 patients reported significant improvements, with half reporting a return to normal energy levels. DAILY STAR - ME sufferers have been offered new hope following a landmark study which suggests the condition can be reversed with counselling and exercise. - The ground-breaking study is the most comprehensive to date and challenges the widely accepted belief that the illness cannot be cured. In this climate of spin and propaganda which worked against the medical and social needs of M.E. and CFS patients, perhaps the NICE guideline should not only aim to be accurate and reliable, but also go even further towards counteracting the propaganda that has indoctrinated the public, doctors and the media. Something that might help would be to define some of the pathology of the diseases. Although the causes of M.E. remain unknown there is abundant established and published pathology. If the guideline included even a short list of some of these pathologies it might encourage doctors to believe patient's accounts of their symptoms and disability. The list could include factors such as: reduced blood volume, reduced cerebral blood flow and regions of cerebral hypo-perfusion, altered gene expressions, oxidative stress and impaired mitochondrial function, cell-free DNA levels commensurate with significant illness, other inflammation, gene expressions, excess lactic acid, etc., etc. Including a list of pathologies would also help doctors and patients who are confused by the sheer range of possible symptoms, to understand that those symptoms can originate from known M.E. and CFS pathology, and not from theories	

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				about a patient's mentality, morality or fitness. For patients and doctors, this evidence based information could contribute more to eliminating prejudice, than pages of questionable opinions about Energy Management and CBT.	
VIRAS	Guideline	General	General	The Myalgic encephalomyelitis: International Consensus Criteria (ICC. 2011) states that diagnostic symptoms of M.E. can include: "urinary urgency or frequency, nocturia" (https://pubmed.ncbi.nlm.nih.gov/21777306/), and the Canadian Clinical Working Case Definition (CCC 2003) includes: "urinary frequency and bladder dysfunction" as well as "Interstitial Cystitis, Irritable Bladder Syndrome". (https://www.tandfonline.com/doi/abs/10.1300/J092v11n01_02). And the USA CDC define symptoms, "commonly present in people with ME/CFS", as including "urinary symptoms". (https://www.cdc.gov/me-cfs/programs/evidence-review.html) It would be helpful if doctors and patients are aware that bladder symptoms are common features of the M.E. and CFS symptom complexes.	Thank you for your comment. Genitourinary system disorders is included as a category in the examples of co-existing conditions seen in people with ME/CFS in the discussion section of Evidence review D-Diagnosis.
VIRAS	Guideline	General	General	The Energy Management section is dubious. Despite explanations to the contrary, the claims made portray an established and authoritative approach which readers would be justified in believing, can give patients control over their illness and improve their symptoms. The inclusion of these 'comforting lies' (Vonnegut) and intrusions into how patients choose to dispense their limited energy threatens patient autonomy and their right to Informed Consent because the risks have not been researched or stated. Adhering to concepts of Energy Management might isolate a patient from their support network and deprive them of other resources that help them to cope. The concept appears to assume that patients have not adapted with the best coping strategies for their individual circumstances, and that they must	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the commissioned report on children and young people) and their own experience.

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				accept unfounded advice given without adequate qualifications or warnings. If NICE want patients to cope, a good start would be to rewrite and reframe Energy Management into something much simpler, less formulaic and with appropriate cautions that recognise that patients are autonomous human beings. The guideline could include directions to additional sources of information on the topic for those who want to investigate further. Patients that choose to investigate more complex and formal Energy Management for themselves can make their own choices without their doctor (or NICE) becoming an inadvertent cause if something goes wrong.	This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and this applies to all the recommendations in the guideline. This is followed by a link to 'Making decisions using NICE guidelines' and this explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.
VIRAS	Guideline	General	General	For around three decades, certain doctors and psychiatrists with links to medical reinsurance companies*, have dominated the medical and social narrative of Myalgic Encephalomyelitis, reinventing a neuro-immune disease as a psychosocial condition of neurotic and phobic hypochondriacs. Their success is evidenced by the draft guideline itself, because 65 years after the Royal Free Hospital outbreak, NICE do not have a single	Thank you for your comments and information. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses. The importance of using clinical judgment when deciding on additional

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				diagnostic test or treatment to recommend. Instead it provides for Energy Management which might save a few patients from deteriorating, and CBT to enable some patients to adapt to living with a disease that could blight the rest of their lives. In this sad situation misdiagnosis with M.E. would be a tragedy, especially if the true cause of a patient's illness was treatable. This exact scenario has played-out numerous times as the following evidence will show, yet the draft guideline does not even provide a list of the most important and/or likely conditions to be investigated and excluded. High on such a list would be Lyme disease because of the significant symptom overlap, as demonstrated when VIRAS surveyed 20 M.E. patients using the Isabel Symptom Checker, (https://symptomchecker.isabelhealthcare.com/). To use the symptom checker, a list of symptoms is entered and an ordered list of possible conditions is presented. 10 (50%) of M.E. respondents had 'CFS' and 3 had 'Lyme disease' given as their number one suggestion. Overall, 12 respondents had Lyme disease included in the top 3 suggested conditions that could cause their symptoms and for 14 respondents Lyme was in the top 5. Lyme disease is only covered in the NICE Evidence Review 4. But there is justification to include this specific infection in the main guideline because the threat to patient safety is inevitable and foreseeable. In a VIRAS survey of 130 UK Lyme disease patients, 62% had previously been diagnosed with either M.E. or CFS. (https://www.facebook.com/groups/125009824843872/permalink/141541083190746/) Lyme disease and its common co-infections must be considered and reconsidered to ensure that a treatable infection is not being	investigations is emphasised. The examples are not intended to be an exhaustive list. As you note infections and infection- related disorders is included as a category in the examples of differential diagnoses and co-existing conditions seen in people with ME/CFS in the discussion section of Evidence review D-Diagnosis. The examples include Lyme disease and post-Lyme syndrome.

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				overlooked. Failure to do so might allow the infection to progress causing serious and avoidable injury and disability. E.g.: England Rugby player Matt Dawson suffered heart injury from a Lyme infection that was left undiagnosed and untreated for too long. (https://www.bbc.co.uk/news/health-40973709 & https://metro.co.uk/2018/08/01/former-england-rugby-captain-describes-catching-lyme-disease-tick-bite-park-7786707/) American actor and musician Kris Kristofferson was diagnosed with Fibromyalgia then early onset Alzheimer's, but when he was finally diagnosed and treated for Lyme disease, his symptoms improved. (https://www.huffpost.com/entry/a-slow-slipping-away-kris-kristoffersons-long_b_577c047be4b00a3ae4ce6609 & https://www.rollingstone.com/feature/kris-kristofferson-an-outlaw-at-80-183141/) Eight insurance companies recently settled with a group of 24 Lyme disease patients in a law suit (Torrey vs. IDSA US) brought against them and seven members of the Infectious Disease Society of America (IDSA) who were responsible for the IDSA Lyme disease Guidelines. E.g., the Lyme Resource Centre reports: (http://www.lymeresourcecentre.com/news/979) "The lawsuit contends that: • "There is sufficient evidence to establish that the IDSA panelists were paid by, and influenced by, insurance companies." • "A large number of patients, at least 20 percent, do not respond to short-term antibiotic treatment." • "chronic Lyme disease patients who do not respond to short-term antibiotic treatment, and do not receive long-term antibiotic treatment, will suffer debilitating symptoms,	

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				will be in constant pain, will be unable to function or live a normal life, and will eventually die from Lyme disease." "We hope this will now allow the mounting emerging science to come to the fore, which undoubtedly shows that standard antibiotics, in particular doxycycline, fail to kill the Lyme spirochete in animal and test-tube experiments. Published research also acknowledges that 10 to 20 percent of early treated patients remain ill under current short-course protocols such as recommended by NICE. "Although the insurers have settled, the suit against the other defendants will continue." The NICE Evidence Review 4 states: "The committee took the view that an exhaustive list of all possible conditions which might be considered was not possible, nor was it appropriate to provide advice on these conditions in this guideline, where there is relevant NICE guidance it is referenced in the recommendations." Listing the more probable possible conditions which could be overlooked would be helpful in the main guideline, and could prevent missed or misdiagnosis for some patients. Furthermore, the statement above fails to take into account the quality of the evidence used in preparing NICE guidance and this is particularly apposite to its Lyme disease guideline. The NICE committee and Stakeholders for the M.E. guidelines might be interested to know that the NICE guideline for Lyme Disease (NG95) provides 12 major items of information and recommendations: "Based on the experience and opinion of the Guideline Committee", three major recommendations: "Based on very low quality evidence" and just one: "Based on moderate to very low quality evidence". That covers virtually all of the	

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				guidance. The result is a guideline with no evidence base and which represents nothing more than the opinions of a committee with minimal knowledge and experience, which has incautiously adopted the position of the USA IDSA. 'Evidence based' it most certainly is not. (https://www.bmj.com/content/361/bmj.k1261) Lyme borreliosis is under-diagnosed in the UK. Many doctors and the public do not recognise the risk factors, signs or symptoms of the disease. Examination and standard blood tests of infected patients frequently show no specific abnormality. Yet patients who remain chronically infected must eventually get a diagnosis of something. Given the symptom profile overlaps and the lack of an alternative explanation for a Lyme patient's symptoms, a highly likely diagnosis is ME/CFS. In an online survey of 330 Lyme borreliosis patients conducted by VIRAS (https://www.facebook.com/groups/125009824843872/permalink/141541219857399/) 78% of patients experienced long delays in getting tested for Lyme disease because "My doctor thought the symptoms were something else". The next highest factors in delaying testing were: "My doctor did not know about Lyme disease", then, "I did not know about Lyme disease". In the same survey, only 27% of respondents had a known or suspected tick bite, 23% had a diagnostic Erythema Migrans rash, and only 10% had both. This meant that the health of many of these patients depended on a doctor making a correct interpretation of their symptoms. The alternative is that patients are given a misdiagnosis or left to carry out their own investigations without the support of the NHS. In *The Complete Guide to Chronic Fatigue Syndrome,* author Dr Katrina Berne, lists 145 symptoms which can occur in patients with ME/CFS. In another VIRAS survey of 130 UK Lyme disease	

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				patients, 62% had previously been diagnosed with either M.E. or CFS, and 70% of respondents indicated having 20 or more symptoms selected from a limited list. (https://www.facebook.com/groups/125009824843872/permalink/141541083190746/) Dr Richard Horowitz produced a 38 point symptom checklist for Lyme disease. M.E. expert doctors and patients will recognise the significant overlap with M.E. symptoms: (https://www.lymedisease.org.au/horowitz-msids-38-point-symptom-checklist/) 1 Unexplained fevers, sweats, chills, or flushing 2 Unexplained weight change…..loss or gain 3 Fatigue, tiredness 4 Unexplained hair loss 5 Swollen glands 6 Sore throat 7 Testicular pain / pelvic pain 8 Unexplained menstrual irregularity 9 Unexplained breast milk production, breast pain 10 Irritable bladder or bladder dysfunction 11 Sexual dysfunction / loss of libido 12 Upset stomach 13 Change in bowel function (constipation or diarrhea) 14 Chest pain or rib soreness 15 Shortness of breath / cough 16 Heart palpitations, pulse skips, heart block 17 History of heart murmur or valve prolapse 18 Joint pain or swelling 19 Stiffness of the neck or back 20 Muscle pain or cramps 21 Twitching of the face or other muscles 22 Headaches 23 Neck cracks or neck stiffness	

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				24 Tingling, numbness, burning or stabbing sensations 25 Facial paralysis (Bells palsy) 26 Eyes/vision – double,blurry 27 Ears/hearing – buzzing, ringing, ear pain 28 Increased motion sickness, vertigo 29 Lightheadedness, poor balance, difficulty walking 30 Tremors 31 Confusion, difficulty thinking 32 Difficulty with concentration or reading 33 Forgetfulness, poor short term memory 34 Disorientation; getting lost, going to wrong places 35 Difficulty with speech or writing 36 Mood swings, irritability, depression 37 Disturbed sleep – too much, too little, early awake 38 Exaggerated symptoms or worse hangover from alcohol Unlike many other chronic conditions, both ME/CFS and chronic Lyme borreliosis can present with a bewildering array of symptoms affecting virtually any organ or system, including the immune system. Overlooking a Lyme disease infection and diagnosing ME/CFS is serious and common. This medical error not only impacts patients lives, it also represents a potentially huge financial cost. Easy to diagnose signs suggestive of the presence of Lyme disease are comparatively rare in the UK. Lyme arthritis is rare with European strains of Lyme borreliosis and present in less than 1% of cases. Lyme carditis is rare and presents in only 1% of UK Lyme cases. Acrodermatitis chronica atrophicans is rare in the UK, and occurs in less than 1% of cases. Even the over-emphasised diagnostic erythema migrans rash, occurs in only around 25% of cases as initially established by the CDC before the cause of Lyme disease was even discovered (https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/infectious_diseases/lyme/1976circularletterpd	

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				f.pdf). Knudtzen et al (March 2017) analysed 431 confirmed cases of Lyme neuroborreliosis of which 37% reported a tick bite and only 20% had an Erythema Migrans rash. (https://doi.org/10.1093/cid/cix568) Overestimates of the incidence of a bulls-eye rash, has probably contributed to many cases of infection being overlooked, yet without treatment, many of those infections will go on to cause chronic illness. The USA National Institute of Health, Tick Borne Disease Working Group report to Congress states that 10%-20% of treated cases remain chronically ill. (https://www.hhs.gov/sites/default/files/tbdwg-report-to-congress-2018.pdf) Obviously, it is unknown what percentage of infected but undiagnosed and untreated patients become chronically ill. In 2018, VIRAS produced a highly conservative estimate for the incidence of Lyme disease in England and Wales based on authoritative sources of information, of between 15,000 and 45,000 cases per year. Cook and Puri recently estimated that the UK incidence of Lyme disease could be as high as 132,000 per year, according to human sero-prevalence and canine sentinel data. (https://doi.org/10.1016/j.idm.2020.10.004) Compared to the officially identified cases by Public Health England of around 1,000 cases in England and Wales with an additional estimate of 2,000 cases unaccounted for, Lyme disease in the UK is evidently not being diagnosed or treated. (https://www.facebook.com/groups/125009824843872/permalink/256178015060385/) Therefore, amongst UK patients diagnosed with ME/CFS there are undoubtedly a substantial proportion of unrecognised cases of Lyme borreliosis. Doctors and patients must be warned about the risks.	

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				*Hooper & Williams. MAGICAL MEDICINE: HOW TO MAKE A DISEASE DISAPPEAR. Feb 2010. Online at: http://www.margaretwilliams.me/2010/magical-medicine_hooper_feb2010.pdf	
VIRAS	Guideline	024 - 026	001 - 015	The Energy Management section (p.24) overlooks a number of important points. The risks of energy management are not considered. Despite some wording to the contrary, the section claims that the approach helps patients to 'stabilise', to 'increase tolerance' or to 'increase activity' and that it can achieve 'goals'. There is no good evidence to substantiate these claims. The unfounded claims imply that patients can control the illness and are able to effect improvement. A logical extension is that if patients do not stabilise or if they deteriorate, it must be their own fault because they are not doing Energy Management properly. The NICE Evidence review G points out that, "Although research on pacing is sparse, this method of activity management is preferred by many people with ME/CFS," and others have claimed that, "in several large patient surveys the majority of respondents found pacing to be helpful" (https://me-pedia.org/wiki/Pacing), and that Pacing is "popular with patients" (https://hansard.parliament.uk/Commons/2003-06-09/debates/ad79a919-d0e1-4af4-98c7-5ac55e50ef57/Me). After conducting a thorough Evidence Review which exposed serious weaknesses in the quality of evidence from research into non-pharmacological interventions, NICE then choose to promote Energy Management because some surveys of self-selected participants suggest that they prefer Pacing. Neither NICE nor anybody else, other than the individual respondents - know what each one considers 'Pacing' actually is – nor whether	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits. This section of the guideline provides information on the principles of energy management and is clear that it includes all types of activity (cognitive, physical, emotional and social) and takes into account their overall level of activity. Energy management uses a patient led flexible, tailored approach so that activity is never automatically increased but is maintained or adjusted (upwards after a period of stability or downwards when symptoms are worse). (see Evidence review G for the committee discussion on self-management strategies). The committee note that care for people with ME/CFS is personalised and any activity is tailored to their circumstances with the support of ME/CFS specialist care. The committee agree that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment

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				or how they practice it in their daily lives nor whether it is authentically helpful. Informal pacing is something that many patients work-out for themselves and use when and to the extent that fits with their circumstances and preferences. So patients might SAY that they prefer Pacing, but in reality they have simply adapted activities in a way that accommodates their needs and wishes without causing too much PEM. When it comes to the reality of adopting even an individualised energy management programme, patients will soon discover that it is impossible to adhere to, particularly amongst those with 'Severe' or 'Moderate' M.E. Adopting the strategy could actually deprive patients of the very activities that give them some quality of life, some sense of purpose and meaning. Activities that allow them to maintain a job or a home or relationships. The NICE advice appears to suggest that a mother of young children must stop and rest whenever she feels like her 'energy envelope' is empty, or tells a father to have a little nap while his kids are waiting for him to pick them up from school, because he overdid it pushing a vacuum cleaner around. Perhaps a patient should not have sex, even if they are really in the mood after weeks of abstinence, because it could make their symptoms worse for several days? Or maybe a patient cannot visit their family because it would push them over their personal limit? (Something that Covid-19 has highlighted is how much people value visiting family and friends and the cost of missing those opportunities). Perhaps some patients will not be able to go to their place of worship because it does not fit into their Energy Management plan. The micro-management expected of patients to follow even a relaxed Energy Management plan, suggests that patients are like hamsters who can spend two minutes on their wheel before	and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care. *Pacing* The committee discussed the use of the term pacing agreed that it means something different to different people with many different versions in use. The committee agreed that including it would add further to the confusion around this term and for this reason have not included it.

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				being expected to curl-up into a little ball again. But patients are human beings. Although obvious, it seems that this fact is sometimes overlooked by those who consider themselves qualified to prescribe how M.E. and CFS patients should live their lives. Patients are living with the demands of a life blighted by pain and disability and some struggle to find reasons to even go on living. But they also have responsibilities, needs and wishes. They have to find some quality of life wherever they can get it. These realities make even individualised but formulated Energy Management programmes a dehumanising exercise in futility. What probably helps patients is understanding that stressors, whether physical, mental or emotional, that push a patient to their limits, could result in worsening of the illness. Repeated, prolonged or very severe bouts of PEM could be warning signs of protracted or permanent deterioration. If these occur then the stressors should be reduced if possible. Explaining this should be simple. Please be very careful about suggesting that a patient's existence can or should be made subjugate to theories which presume to control their daily lives - while apparently ignoring the reality of human needs and maybe even human rights. Please also be careful about including advice that could brand patients who do not stabilise or improve, or who deteriorate - as people who are not doing their Energy Management properly. This commandeering of patient's lives does not appear to occur in other diseases. But with M.E. it seems that anyone is entitled to impose their opinions about what they 'ought' to do and 'ought' not to do, apparently without questioning whether such overweening intrusions are practical or justified.	
VIRAS	Guideline	004	010	The draft states that M.E. "affects each person differently and varies widely in severity – in its most severe form it can lead to	Thank you for your comment. The committee agree that for everyone with ME/CFS there is an impact on their lives. There is a wide range of impact, there are

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				substantial incapacity (see recommendations 12 1.1.8 and 1.1.9)" The statement could be interpreted as suggesting that 'Mild' or 'Moderate' ME/CFS do not cause 'substantial incapacity'. These unfortunately named severity ratings could already mislead people into believing that patients in these categories are not struggling with life-changing illness. The draft guideline seems to contradict this in the section 'Mild ME/CFS' (p.43,L9): "Most are still working or in education, but to do this they have probably stopped all leisure and social pursuits. They often take days off or use the weekend to cope with the rest of the week." These effects of 'Mild' ME/CFS could be considered 'substantial incapacity' because of the impact they have on patient's lives. Being deprived of all or most leisure and social pursuits is not only a major loss, it is an indication of 'substantial incapacity'. Not being able to go out socially with friends or visit family is already seen by some in Covid-19 lockdowns as a major deprivation. 'Mild' ME/CFS patients might be enduring similar circumstances for many years. Please consider replacing 'substantial incapacity' with 'extreme debility' or use: "Ranges from 'Mild' which prevents patients from doing some important activities, to 'Very Severe' resulting in extreme debility."	people able to carry on some activities and they experience less of an impact on aspects of their lives than people with substantial incapacity and have difficulty with leaving or are unable to leave their homes.. Taking into account the range of comments from stakeholders about the importance of representation for all people with ME/CFS this recommendation has been reworded to reflect the range of impact that can be experienced with ME/CFS. *Definitions of severity* The committee agreed that the impact of severity exists along a continuum and is not easily categorised. However, to provide an overview of the spectrum of ME/CFS definitions of severity have been included at the beginning of the guideline.
VIRAS	Guideline	004	016	"1.1.2 Recognise that people with ME/CFS may have experienced prejudice and disbelief and feel stigmatised by people who do not understand their illness. Take into account: • how this could affect the person with ME/CFS • that they may have lost trust in health and social services and be hesitant about involving them."	Thank you for your comment. The aim of the recommendation was to raise awareness that people with ME/CFS have experienced prejudice and stigma and is based on the evidence identified in the Evidence reviews A and C and the committee's experience. The current wording addresses this. ' People', has been edited to include 'family, friends, health and social care professionals and teachers'.

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				The draft states that, "people with ME/CFS may have experienced prejudice and disbelief…" This statement is unnecessarily politic because there is no question that many patients have experienced prejudice in accessing health and social care and it might be better if the guideline stated this fact plainly. NICE might also consider stating that such discrimination is unacceptable. NICE state that patients may, "…feel stigmatised by people who do not understand their illness". It is strictly true to say, 'people', because prejudice against M.E. and CFS patients can come from almost any quarter. But NICE go on to state that patients, "may have lost trust in health and social services." This "lost trust in health and social services" did not occur because some 'people' judged them to be lazy or hypochondriac and told them they should pull themselves together and do some exercise. Rather, the loss of trust in the medical professions happened because it was health professionals that abused their trust. If NICE cannot grasp this nettle firmly, then patients will continue to encounter discrimination because doctors are famously unable to admit being wrong or to change their opinions. Note what has happened to a doctor who is suffering with long-haul Covid-19: "After working several shifts, I found myself unable to get out of bed one morning: the aches and fatigue were taking over. *"Get up! Push through!"* my mind scolded my body. […] "Provider after provider unknowingly put me on trial, poised to accuse my body of falsification and interrogate it to discover alternate explanations.[…] I apologized for potentially wasting their time, as there might not be anything wrong with me, echoing the hesitancy of many women who are dismissed and fearful of	

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				being labeled as anxious or hypochondriacs." (https://www.statnews.com/2020/10/26/hesitant-identify-myself-as-covid-long-hauler/) This unfortunate doctor is evidently well aware of the pervasive discrimination in healthcare, all too ready to label women as 'anxious or hypochondriacs'. Another long-haul Covid-19 patient wrote: "We long-haulers are also at the mercy of the medical establishment, which has not always responded to our dilemma with sympathy. George, a friend and fellow long-hauler, fought her GP for weeks to get a chest MRI, knowing that her lungs weren't working properly. The MRI revealed she has fibrosis – scarring – in her lungs." (https://www.theguardian.com/commentisfree/2020/jul/26/im-a-covid-19-long-hauler-im-still-dealing-with-pain-fatigue-and-misery) It might be tempting to forget the past and move-on to a new era. Unfortunately the past is still with us. Prejudice of the gas-lighting type remains prevalent, particularly against women and particularly against those with so-called 'mystery illnesses'.	
VIRAS	Guideline	005	005	"take time to build supportive, trusting and empathetic relationships" Please consider removing 'empathetic' from this sentence. Empathy denotes a deep understanding 'as if' sharing in an experience. M.E. patients do not require empathy, they want practical solutions to as many of their problems as possible, the same as patients with any other chronic medical condition. Patients that want mental or emotional support can be referred to counselling. Calling for empathy might be 'positive discrimination', but it is still discrimination which misrepresents patient's needs and wishes. It would almost invariably fail and actually damage trust, if and when the 'empathy' is exposed as	Thank you for your comment. Empathetic is defined as showing an ability to understand and share the feelings of another. This recommendation is supported by the evidence, lack of empathy was reported by people with ME/CFS in Evidence review A, Appendices 1 and 2 and supported by the committee's experience. The committee disagree empathetic should be removed and no changes have been made to the recommendation.

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				disingenuous, time limited, conditional or otherwise inconsistent. Cecchin et al. (1994, p.9)** remark: "Quite often, implicit in this theme of helping is the idea that what people need is warmth, understanding, and, at times, even love. This is an extremely powerful and common prejudice within our culture today, and one that many of us therapists share. How did we get to this absurd position?" ** Cecchin, G., Lane, G. & Ray, W. A. (1994) The Cybernetics of Prejudices in the Practice of Psychotherapy. Systemic Thinking and Practice Series. London: Karnac Books.	
VIRAS	Guideline	022	013	Multidisciplinary care "Provide care for people with ME/CFS using a coordinated multidisciplinary approach. Based on the person's needs, include health and social care professionals with expertise…" Whereas the causes of ME are likely to be multiple, it is paramount that vector-borne infections have not been overlooked in ME patients, and referrals to infectious disease specialists should be a priority. There is a definite possibility that many or all symptoms of ME may be the result of bacterial or viral infections that have not been treated adequately, or not detected, and it is known that that some infections are hard to diagnose by present testing methods. It will be increasingly necessary to realise the financial implications to the NHS, and to individual doctors, of legal actions by patients pertaining to misdiagnosis. A class action lawsuit on behalf of Lyme disease patients has won substantial damages in November 2020 from the Infectious Disease Society of America (IDSA). Further actions are to be taken against 7 individual IDSA doctors due to missed or incorrect diagnoses and treatment of Lyme disease.	Thank you for your comments and information. Throughout the guideline the committee have recommended carrying out investigations to exclude other diagnoses and referral to appropriate specialists. The importance of using clinical judgment when deciding on additional investigations is emphasised. The examples are not intended to be an exhaustive list. As you note in another of your comments infections and infection- related disorders is included as a category in the examples of differential diagnoses and co-existing conditions seen in people with ME/CFS in the discussion section of Evidence review D-Diagnosis. The examples include Lyme disease and post-Lyme syndrome.

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				Some infections, particularly vector-borne infections and parasitic infections, are presently regarded as being so rare that they are not routinely tested for. Failure to recognise their presence most often leads to chronic illness, including post-infection fatigue and many symptoms within the criteria for ME. The committee assumes that adequate criteria exist under NICE guidelines for diagnosing and treating Lyme and chronic infections, and thus assumes that Lyme and tick-borne infections have already been ruled out Page 58, Line 10: " tuberculosis, Lyme disease and post-Lyme syndrome, other chronic infections" https://www.nice.org.uk/guidance/gid-ng10091/documents/evidence-review-4 But it is paramount that the committee acknowledge that, compared with the tools available for diagnosing the other conditions listed (page 58 above), Lyme disease diagnostics are not well established or straightforward. The NICE guidelines for Lyme disease are suitable for managing acute cases but do not encompass chronic cases, and rely completely on unreliable diagnostic tests. Also, it has not been a routine diagnostic procedure in practice to rule out Lyme disease in ME patients. The 2007 NICE Guidelines for ME/CFS did state that the physician must consider ruling out Lyme disease – but there was the caveat that testing was discretionary if the physician believed the patient had a low risk of encountering Lyme borreliosis. However, only a very low number of GPs and consultants have availed themselves of the CME tool on Lyme disease, https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/lyme-disease-toolkit.aspx and when they go through this online CME training course, they will be linked to information from Public Health England stating that the estimated incidence of Lyme disease is only 3,000 cases per year, of which a mere 1000 cases are detected. This is a	

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				gross underestimate which has not been based on the most recent in-depth epidemiological reasoning. 3,000 cases a year would keep Lyme disease almost within the category of rare diseases, whereas 30,000 cases a year estimated by VIRAS, https://tinyurl.com/ybpmnuqf) and 132,000 cases a year (Cook and Puri 2020, (https://doi.org/10.1016/j.idm.2020.10.004) change the whole picture and reveal a disease of some significant risk to the public. The global incidence of tick-borne and other vector-borne infections has increased dramatically over the last 10 years, and even in urban areas in the UK, patients have been infected from a tick in their own back garden or local park. https://www.hackneycitizen.co.uk/2019/08/08/council-warnings-ticks-woman-lyme-disease-clissold-park/ The fact that the predicted incidence of Lyme disease cases could be up to 2 orders of magnitude higher that the number of cases actually recorded, should be a warning sign when considering the thousands of infected patients with no diagnosis, but who are suffering to various degrees with multiple symptoms, and that a high proportion of those patients will quite understandably meet the criteria for ME and/or Fibromyalgia. The hallmark skin rash associated with Lyme borreliosis, and pathognomic for the infection, may be seen in only 60% of cases. https://www.ncbi.nlm.nih.gov/pubmed/21117376 This could be an overestimate, as the original Connecticut epidemic in the 1970s reported that the rash occurred in only 25% of cases. http://www.ct.gov/dph/lib/dph/infectious_diseases/lyme/1976_circular_letter.pdf) It is impossible to know the true incidence of the rash, given that such a high proportion of patients with Lyme borreliosis are never examined in the first few weeks after a tick bite when the rash	

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				might appear, but other more serious symptoms have not become apparent. VIRAS has been regularly and constantly checking not only the biomedical research on ME, but also the social media platforms used by ME patients, for over 15 years. We have found that it is extremely rare for ME patients to have been tested for Borrelia infections, despite the diagnostic criterion listed in the 2007 guidelines. Even more rare is testing for Bartonella, Babesia Ehrlichia/Anaplasma, and Borrelia miyamotoi, all of which are known to be delivered by the same tick bite causing illness in Lyme patients. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004539#sec014 The term Lyme disease should more properly be known as Lyme borreliosis complex, due to the fact that expert doctors and research scientists have shown that 53% of tick-bite victims have at least 1 co-infection, and 30% have 2 or more pathogens as well as Borrelia causing their illness. https://www.lymedisease.org/lymepolicywonk-study-finds-coinfections-in-lyme-disease-common-2/ Two recent surveys of Lyme disease patients by VIRAS (https://www.mediafire.com/file/2wzd0ge3gokjsez/VIRAS_LB_Patient_Survey.pdf/file) and Fight Lyme Now (https://www.linkedin.com/pulse/fight-lyme-now-uk-disease-survey-diagnosis-treatment-cost-newton?fbclid=IwAR3Vg5OLvHXWzKzYDSD4o3Sv6IngrmsMWpvkFsgevQk9-GR66rcQebPxn-8) have shown that a high percentage of Lyme patients were previously diagnosed with ME, and many only discovered that they had Lyme and/or another tick-borne disease after a long time of illness. Their misdiagnoses were often only revealed after they had paid for private tests in highly-accredited but non-UK laboratories.	

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				Primary screening tests for Lyme borreliosis in the UK uses tests which have the disclaimer that a negative result does not rule out the presence of the infection. The sorry state of affairs with respect to Lyme tests in the UK and Europe is summarised by Leeflang et al, 2016 thus "the data in this review do not provide sufficient evidence to make inferences about the value of the tests for clinical practice. " https://doi.org/10.1186/s12879-016-1468-4 and by Cook and Puri, 2020, thus: "For early-stage/acute LD samples, the probability of a false-negative result is 80.3% for a single ELISA test and increases to 85.9% with the two-tier test. This indicates that in early-stage LD, false negatives are 65 times greater than for HIV testing. For late-stage LD, the two-tier test generated 16.7% false negatives compared with 0.095% false negatives generated by a two-step HIV test, which is over a 170-fold difference. Using clinically representative LD test sensitivities, the two-tier test generated over 500 times more false-negative results than two-stage HIV testing" https://doi.org/10.2147/IJGM.S131909 We therefore advise that a more rigorous process is set in place for the investigation of ME patients for vector-borne infections. This is reasonable, in view of the high probability that ME patients, and their doctors, will encounter difficulties with the lack of recognition that these infections are much more prevalent than is generally realised, and that obtaining an accurate diagnosis through the present NHS serology is not totally reliable. Physicians are unfortunately in a difficult position when they cannot rely on the standard serological tests, but they have a duty to avail themselves of the burgeoning information available from the published international literature by experts in the field of tick borne disease. The treatment and care of patients with ME may be better tailored to their needs, once the original infection	

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				from a tick bite has been identified, given that there is much evidence for subtle changes in the immune profile of patients with Lyme or post-treatment Lyme syndrome. https://doi.org/10.3389/fmed.2020.00568	
VIRAS	Guideline	025	001	"'Energy Management' • is a long-term approach - it can take weeks, months or sometimes even years to reach stabilisation or to increase tolerance or activity" How did the Committee rationalise this? If Energy Management can result in improvement it should be evident within a few weeks or months. There is no evidence that patients 'stabilise' or 'increase tolerance to activity' after 'years' due to adopting Energy Management. The implications of controlling patient's behaviour via the advice of a NICE guideline are serious and far-reaching and involve complex ethical considerations, especially in the absence of evidence to support some of the claims NICE have made. Healthy people chose to smoke, drink, stay up too late, eat too much and do not exercise enough, often in the knowledge that sometime in the future, it might prove to be bad for them. The government provide information and recommendations about some of these risks, but nobody presumes to tell people that they cannot make their own choices. Yet because M.E. and CFS patients are treated as though they are incompetent and incapable of governing their own affairs, ordering the minutiae of their lives appears to be acceptable practice. I am a believer that evidence is not always strictly necessary when common-sense and strong critical arguments support an idea. In my opinion, the NICE draft has provided no such arguments for Energy Management and some of its advice appears to be irrational (see below).	Thank you for your comment. *Energy management* Based on the evidence about the lack of information and support people with ME/CFS report in managing their symptoms (Evidence review A) and their experience the committee concluded that people with ME/CFS should have access to personalised advice as part of their care and support plan that supports them to learn to use the amount of energy they have while reducing their risk of post-exertional malaise or worsening their symptoms by exceeding their limits (evidence review G). The committee made consensus recommendations based on the evidence on what people with ME/CFS found useful in managing their symptoms (see evidence reviews A, G and the commissioned report on children and young people) and their own experience

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VIRAS	Guideline	025	025	"1.11.6 Advise people with ME/CFS to reduce their activity if increasing it triggers symptoms, or if they have fluctuations in their daily energy levels." This sweeping advice would predictably require that a substantial proportion of patients do virtually nothing. No shower, no making a cup of tea or sitting up in bed to eat something, no communication with others, no reading, listening to music or watching TV, because any of these activities might 'trigger symptoms'. See the 2007 NICE guideline on what constitutes 'Exercise' and the ICC section on 'Neurosensory' symptoms. Please rethink this advice.	Thank you for your comment. After considering the stakeholder comments this has been edited to,' Advise people with ME/CFS how to manage flare-ups and relapses (see the section on managing flare-ups in symptoms and relapse).'
VIRAS	Guideline	025	027	"1.11.7 Make self-monitoring of activity as easy as possible by taking advantage of any tools the person already uses, such as an activity tracker, phone heart-rate monitor or diary." Some M.E. and CFS patient's lives are hanging by a thread. Patients have experienced many losses through becoming disabled. Relationships may have suffered, their employment or studies could be lost or under threat, they may have lost their home or be struggling to maintain it, they might have had to endure repeated exhausting fights to get state benefits and have been discriminated against in accessing health and social care. Any of these could stretch a healthy person's coping to its limits, let alone someone who is physically and cognitively disabled. Then they are presented with this idea: keep an activity and symptom diary. Put the pain and losses of their miserable existence under a microscope for a few weeks or months, and let them have a good hard look at just how terrible their life has become. Therapeutic counsellors will immediately recognise that this is a potentially catastrophic idea. It could undermine an individual's coping and push them over the limit of what they can endure.	Thank you for your comment. The committee considered the qualitative evidence (Evidence review G-Non pharmacological management) and their experience about the benefits of people using tools to monitor activity alongside the potential harms of increasing their burden and causing anxiety about activity levels. On balance the committee agreed it was important that self-monitoring of activity was acknowledged and where used it should be as easy as possible. The committee agreed that the issue of choice is fundamental to patient care. At start of the guideline the guideline links to the NICE page on 'Making decisions about your care' this underpins the importance of people being involved in making choices about their care and shared decision making. The importance of choice and person centered care is directly reinforced in the guideline sections approach to delivering care and assessment and care planning. It is made clear that the person with ME/CFS is in charge of the aims of their care and support plan and that they can withdraw or decline from any part of their care and support plan without it affecting access to other aspects of their care and this includes the use of self- monitoring techniques.

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				There is a real risk of distress, depression and perhaps even suicide with this ill-thought-out approach, and I do not believe that the dangers would be averted by regular or close monitoring by a health professional if they do not understand grief, coping, and loss of identity.	
VIRAS	Guideline	034	006	"CBT should be only delivered by a healthcare professional with appropriate training and experience in CBT for ME/CFS" This requirement would automatically disqualify many if not all CBT therapists who are already trained and who 'have experience in CBT for ME/CFS'. Before the new guideline is published and becomes policy, CBT therapist's experienced with M.E. clients, will probably have been working based on the 2007 NICE Guideline and the much publicised 2011 PACE Trial. Who is going to inform them that they have been doing it wrong and retrain them to do it properly? What will be done for patients who have lost faith in healthcare, because their CBT was actually abusive (even if the patient never realised it), being based on false premises and impossible expectations? These problems could be addressed by removal of CBT from the draft, and replacement with advice that some patients might require counselling or other mental health intervention, in order to cope with the life-changing restrictions imposed by the disease.	Thank you for your comment. The committee agree that training for health and social care professionals is important and have recommended that health and social care providers should ensure that all staff delivering care to people with ME/CFS should receive training relevant to their role and in line with the guideline. To note the training recommendations have been edited. . *CBT* Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). After reviewing the evidence for psychological and behavioural interventions other than CBT the committee concluded that although some benefit was reported for different types of interventions the evidence was mainly based on single studies and the evidence was low to very low quality. The committee agreed that there was insufficient evidence to make any recommendations for any of the interventions (see evidence reports G and H).

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VIRAS	Guideline	034	002 + 014	"Only offer cognitive behavioural therapy (CBT) to people with ME/CFS who would like to use it to support them in managing their symptoms of ME/CFS" and, "improve functioning and reduce the psychological distress associated with having a chronic illness" There is no evidence which shows that CBT can 'manage symptoms' or 'improve functioning' for M.E. or CFS patients. The draft claims that CBT can, "reduce the psychological distress associated with having a chronic illness". There is no evidence that CBT is any better than any other approaches intended to reduce psychological distress for patients with M.E. or CFS. Patients with M.E. and CFS have been repeatedly shown to have the lowest quality of life out of numerous serious chronic conditions.** It has never been established how much of that burden is due to pain and disability, how much is due to the losses that the illnesses imposes, and how much is due to stigma and discrimination. There is reason to believe - based on many years of evidence from patient's accounts and negative representations of patients in the media, that singling-out and promoting CBT for any purpose, could perpetuate the avoidable added burden and long-standing disgrace of discrimination against patients. Making misleading claims for what CBT can achieve for patients appears like more of the same. The committee might consider the problem that with a recovery rate of only ~5%, that by any criteria there are already tens of thousands of very long-term patients. Any of those patients would be entirely justified in rejecting any form of CBT regardless of the claimed purpose or aims, based on what they have	Thank you for your comment. *Decision making* One of the strengths of NICE guidelines is the multifaceted approach taken in developing the recommendations. Recommendations in NICE guidelines are developed using a range of evidence, in addition to this guideline committees are formed to reflect as far as practically possible, the range of stakeholders and groups whose activities, services or care will be covered by the guideline. When developing this guideline the committee considered a wide range of evidence, including that from, published peer review quantitative and qualitative evidence, calls for evidence for unpublished evidence, expert testimonies, and two commissioned reports focusing on people with ME/CFS that were identified as underrepresented in the literature. As with all NICE guidelines the committee uses its judgment to decide what the evidence means in the context of each topic and what recommendations can be made and the appropriate strength of the recommendation. The committee will consider many factors including the types of evidence, the strength and quality of the evidence, the trade-off between benefits and harms, economic considerations, resource impact and clinical and patient experience, equality considerations. (See Developing NICE guidelines: the manual, section 9.1 for further details on how recommendations are developed). Based on the quantitative and qualitative evidence (evidence reviews G and H) and their own experience the committee concluded that CBT could be offered where this is appropriate and chosen by the person with ME/CFS to help them manage their symptoms and reduce the distress associated with having a

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				personally experienced and witnessed. What do NICE propose doing for them if their coping fails? CBT could be replaced with 'supportive therapy' which can be defined as, 'developing coping skills and strategies, in collaboration with a trained professional'. All of the unfounded claims for what this could achieve should be removed from the guideline. ** The Health-Related Quality of Life for Patients with Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS). PLoS ONE 10(7): e0132421. (2015).	chronic illness. The committee concluded it was important to accompany these recommendations with ones that set out how CBT should be delivered for people with ME/CFS. (See evidence reviews G and H for the evidence and the committee discussion on these recommendations). As part of this the aim of CBT is to improve quality of life, and this includes functioning and some of the evidence supported this (see evidence review G).

Document processed	Organisation name – Stakeholder or respondent	Disclosure on tobacco funding / links	Number of comments extracted	Comments

None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.
