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INVEST IN ME
RESPONSE TO INSTITUTE OF MEDICINE DOCUMENT
"Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness"

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The report published by the Institute of Medicine (IOM) entitled "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness" [1] was published in February 2015.

Invest in ME have read the full document and submit the following comments about the report.

Invest in ME

Invest in ME (IiME) is a UK charity (charity number 1114035) established in 2006 to educate the public and media about Myalgic Encephalomyelitis (ME) and raise funds for fundamental biomedical research into ME. We have links internationally and are current chair of the European ME Alliance, an umbrella organisation of 13 national European patient groups working together to improve awareness of ME. IiME have so far organised nine annual international ME/CFS conferences and four research colloquiums in London, UK, to allow researchers, clinicians, patient groups and patients to learn about the latest research, form collaborations and share experiences to advance research into this condition.

The charity strongly believes in international biomedical research collaboration and have initiated possibly the two most important research projects for ME in the UK – a gut micriobiota study [2] and a project leading to a UK clinical trial using rituximab to treat ME patients [3].

In the UK patients prefer to use the term Myalgic Encephalomyelitis - **ME -** as it has over fifty years of history behind it and is already recognised by the World Health Organisation**.**

In this document we'll use **ME/CFS** from here on to match the IOM terminology and also that used in the Canadian Consensus Criteria for which IiME is UK distributor of the printed version).

Below are comments that we have concerning the IOM document.

We conclude this document with a summary and our recommendations.

Invest in ME – Response to IOM Report

The purpose of this IOM report was

> *".. to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge."*

The report states that

> *"A number of reviewers were asked for comment but "they were not asked to endorse the report's conclusions or recommendations, nor did they see the final draft of the report before its release."*
>
> *"Responsibility for the final content of this report rests entirely with the authoring committee and the institution."*

Prior to this report being initiated Invest in ME had commented that this work was not necessary [IiME response - http://www.investinme.org/IIME%20Statement%202013-11-01.htm]

Our reasons for criticising the planned IOM report at the time were that we wished to support the statement signed by 50 clinicians and researchers [4] who were involved in ME or CFS related research and in the treatment of patients and who "strongly urge the Department of Health and Human Services (HHS) to follow our lead by using the CCC as the sole case definition for ME/CFS in all of the Department's activities related to this disease".

Our fears were based on experiences in UK where NICE produced guidelines for ME/CFS which were mediocre and unfit for their purpose. The IOM seemed to have little knowledge of the true experience of ME/CFS and the funding used for the study could have been used for biomedical research into ME/CFS. Adoption of the CCC as a standard set of guidelines, although not perfect, could have moved things on immediately and left much of the poor research and the vested interests in ME/CFS behind. The IOM had also just concluded a poorly received analysis of the Gulf-War Syndrome.

Our view was, therefore, clearly the correct policy at that time.

But the ethos of IiME is to look for positives and opportunities. The IOM report was made and we will comment honestly regarding our view of the results.

IOM Brief

The study was sponsored by many agencies of the Department of Health and Human Services and conducted by a committee convened by the Institute of Medicine (IOM) – [This study was supported by Contract No. HHSN263201200074I between the National Academy of Sciences and the National Institutes of Health]
To conduct this study, the IOM convened the Committee on Diagnostic Criteria for ME/CFS.
The committee was asked

- to define diagnostic criteria for myalgic encephalomyelitis/chronic fatigue syndrome
- to propose a process for re-evaluation of these criteria in the future
- to consider whether a new name for this disease is warranted

"*for this complex, multisystem, frequently undiagnosed, often life-altering condition*."

The IOM committee recommended "*an evidence-based, disinterested procedure by which these criteria can be refined in the future on the basis of new research*."
The committee also conducted a literature review on ME/CFS research.

The HHS sponsors charged the committee with evaluating the current criteria for diagnosis of ME/CFS and recommending clinical diagnostic criteria that would address the needs of health care providers, patients, and their caregivers.

Specifically, the committee was asked to

- conduct a study to identify the evidence for various clinical diagnostic criteria for ME/CFS using a process with input from stakeholders, including practicing clinicians and patients;
- develop evidence-based clinical diagnostic criteria for ME/CFS for use by clinicians, using a consensus-building methodology;
- recommend whether new terminology for ME/CFS should be adopted;
- and develop an outreach strategy for disseminating the new criteria nationwide to health professionals.

The committee was also asked

- to distinguish among disease subgroups,
- develop a plan for updating the new criteria,
- and make recommendations for the plan's implementation

The statement of task requested that the committee's recommendations consider unique diagnostic issues facing people with ME/CFS related specifically to gender and particular subgroups with substantial disability, and extending across the life span.

The committee **was not asked** to investigate the aetiology, pathophysiology, pathogenesis, or treatment of ME/CFS.

The IOM report follows publication of the P2P report [5] which IiME commented upon [6].

These two reports need to be seen together to establish a broader view of ME/CFS and of the workings of those who have been charged to produce an update on research, treatment and perception of ME/CFS.

For the P2P report it was easier to comment in a sequential manner to the report.
The IOM report is different in that it contained several sections and embedded the results of a literature review.

The report was sectioned into Background on ME/CFS including its history, its terminology, and its burden and impact, Current Definitions and Diagnostic Criteria, Review of Evidence of Major and Other Symptoms, Paediatric ME/CFS and Recommendations. A plan for dissemination of new criteria to health professionals was also included

Our response, therefore, consists of observations from reading the full report followed by a summary of conclusions and comments.

Literature Review

The committee conducted a comprehensive literature review which we feel was, in the end, a valuable exercise.
The committee conducted a literature search for all articles published since 1950.
However, "*the committee reviewed only papers published during the last 10 years with the understanding that the older research is considered and cited in the introduction and discussion sections of more recent literature*."

The review may be criticised for not being comprehensive enough, for including doubtful research from some quarters or leaving other, newer research out of the review – but there will always be the risk behind performing such an exercise in a context where the patient population has been so poorly served by establishment organisations controlling research budgets or managing perceptions about ME.

This is also understandable as the technology changes quite rapidly and very old research papers may not be comparable with the newer ones.

The literary research was, we feel, a good exercise to perform and provides a base for additional research to be analysed going forward.

Proposed Diagnostic Criteria for ME/CFS

The IOM committee proposed a revised set of criteria for diagnosing ME.
Final recommendations regarding diagnostic criteria were made by consensus after deliberation by the committee as a whole. The committee decided that new diagnostic criteria, which they believed focused more on the central symptoms of ME/CFS than many other definitions, were warranted for this disorder.

1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is 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,

2. Post-exertional malaise,* and

3. Unrefreshing sleep*

With at least one of the two following manifestations is also required:

1. Cognitive impairment* or

2. Orthostatic intolerance

* Frequency and severity of symptoms should be assessed. 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.

The proposed criteria are, on the surface, very simple and the risk is that these are too broad. But the committee also added a table with many more criteria which could be used to support the diagnosis.

Whilst it may be good that a set of simplified criteria are produced there is the concern that the criteria listed by the IOM report may be too light.

It would require education of doctors to make them able to identify the disease and avoid incorporating misdiagnoses into the assessment. The multiple comments within the IOM report relating to lack of belief from healthcare staff are evidence that this education is important.

It should be noted that the Ramsay criteria were simple as well and we understand the IOM criteria are meant to be clinical criteria and research criteria would be different.

IiME also believe that we need centres of excellence that can take responsibility for the disease as it is not satisfactory to leave ME/CFS patients to be diagnosed and treated by primary care practitioners only.

The committee recognised that some patients diagnosed by other criteria such as Fukuda would not fulfil all of the criteria proposed in this document but emphasized that all patients should receive appropriate care.

> *"Case definitions work well for illnesses for which the underlying pathology is understood and can be observed; establishing the presence of disease-specific pathology through examination or testing provides a gold standard for diagnosis of a particular disease, and potential case definitions can be compared against this standard."*

As case definitions work best for illnesses for which the underlying pathology is understood and can be observed then it is all the more important to fund research that has the possibility of finding reproducible biomarkers to aid the diagnostic process.

At the IiME conference in 2014 the topic of criteria arose and Dr Julian Blanco said that he did not see any problem in large studies across countries or within countries as the researchers will identify similar patients. Most researchers now use the CCC for research purposes. He saw the problem with diagnostic criteria being different in different countries and people not being well diagnosed. He also said that for treatment purposes it is important to stratify clinical data as not all patients are the same and treatments should be done in a clinical trial setting with data being collected so that the results can be published and shared. So his message was that as long as the patients are diagnosed in a similar manner researchers are able to choose the right kind of patients to use for research purposes.

Diagnostic criteria are important for health policy purposes, social security etc. and they cannot be as tight as research criteria.

We are not interested in studying the disease in isolation. All research into ME/CFS, using the same recognised up-to-date criteria (such as CCC), need to play a role in the total strategy with a view to be shared by other researchers.

If the ME/CFS diagnostic criteria, due to lack of identifiable biomarkers, are more useful for preventing or managing the illness then it is important that health care providers are informed about the importance of listening to the patient and giving common sense advice instead of prescribing CBT and GET as first line treatments as has been done in the UK.
It is also all the more important to support clinical trials (such as the rituximab trials in Norway [7] and UK [3] in order to learn about the disease from the outcomes from treatment.

We welcome the recommendation that these guidelines should be revisited within five years. We would connect this to our recommendation in the P2P report that a 5 year funding program of $250 million is given to biomedical research into ME and that it is revisited after 5 years.

The Name

The name of this illness was commented on early in the report.

For many the name has always been a contentious issue – understandably so when establishment organisations and individuals with vested interests have for so long manipulated the way this disease is perceived, funded and researched.

It is important to restate that the IOM brief was to consider whether a new name for this disease is warranted – there was no necessity to change the name.

IiME's view has been a pragmatic one – that the name will eventually take care of itself once enough data has been collected from proper research. Until that time then the current name, registered with WHO as myalgic encephalomyelitis, would be the name of choice.

Any suggestion to change the name has, we feel, many consequences. At this time this subject has to be approached carefully.

The IOM committee stated that -

> *"After extensive consideration and mindful of the concerns expressed by patients and their advocates, the committee recommends that the disorder described in this report be named "systemic exertion intolerance disease" (SEID). "Systemic exertion intolerance" captures the fact that exertion of any sort—physical, cognitive, emotional—can adversely affect these patients in many organ systems and in many aspects of their lives. The committee intends for this name to convey the complexity and severity of this disorder."*

The IOM report stated -

> **"***the committee determined that the name "chronic fatigue syndrome" has done a disservice to many patients.***."**

This is good news to hear from an influential body and follows on from similar statements in the P2P report.

This now effectively means that CFS is redundant.

The only reason that ME/CFS is used is due to the connection with the CCC guidelines.

However, we take issue with the view of the IOM committee -

> **"…***that the name "myalgic encephalomyelitis" does not accurately describe the major features of the disease"*

The committee deemed the term "myalgic encephalomyelitis," although commonly endorsed by patients and advocates, to be inappropriate because of the general lack of evidence of brain inflammation in ME/CFS patients, as well as the less prominent role of myalgia in these patients relative to more core symptoms.

We disagree entirely with this viewpoint.

"Listen to Patients"

The IOM committee states that it was "*mindful of the concerns expressed by patients and their advocates*" but we feel they have partially ignored this.

In a report which later continually confirms the paucity of research and the possibility that new research can change things then it seems senseless to us to make a change to the name of this disease at this time, and somewhat irresponsible.

It also seems a little odd to suggest a name change when the report also states –

> *"The committee was not asked to investigate the etiology, pathophysiology, pathogenesis, or treatment of ME/CFS."*

Caution would be the best option in this instance and would advise against a short-term approach to change the name.

The report later commented -

> *"The committee expects that this research will lead to findings that can be used to further refine the diagnosis of this disorder and the elaboration of clinically pertinent subtypes."*

The report also ignores obvious evidence that it quoted –

> *"Comments submitted to the committee also noted that other illnesses, such as Parkinson's disease, are not named after their symptoms. Patients often pointed out that ME/CFS, which includes symptoms in multiple systems that occur for an extended period of time, involves much more than fatigue, a level of complexity and impact not conveyed by the term "chronic fatigue syndrome."*
> *"Many respondents objected specifically to the use of "fatigue" in the name because they do not believe fatigue to be the defining characteristic of this illness."*

This also underlines why a name change, especially one which contains the term exertion, is premature as no name using a fatigue-related description will be adequate.

So we wonder why there is a judgement to suggest a change of the name now as expected research findings will surely provide more clarity regarding nomenclature.

> "However, there remains disagreement as to whether ME and CFS are separate conditions or are similar enough to belong under an umbrella term such as ME/CFS."

Dr Ramsay's criteria, which some in the UK consider to be 'classic' ME, had a hall mark symptom of muscle fatigability after minimal physical effort and delayed recovery. This document seems to have taken this symptom into account when discussing the new name SEID but gone further than just physical activity causing delayed recovery and included fatigability after mental and emotional effort as well.

The IOM report stated -

> *"Reaching consensus on a name for this illness is particularly challenging in part because its etiology and pathology remain unknown (CFS/ME Working Group, 2002)."*

Yet this does not preclude this occurring for other diseases which have similar constraints.

At this stage it would have been better to leave ME in the name and wait for the required new evidence within the next five years. Even the UK MRC now (finally) accepts that there is evidence of neuro inflammation in some severe cases of ME [8].

Whilst we welcome the acknowledgement of the systemic nature of ME and that it is a disease – both points which need to be distributed to healthcare professionals - IiME feel the overall effect of the recommendation to change the name is inappropriate.

The report states -

> *"Unfortunately, the word "fatigue" does not convey information about the cause, severity, or chronicity of fatigue or its impact on functionality."*

Yet neither does" Exertion". In fact the report also states -

> ***"Conclusion:** There is sufficient evidence that fatigue in ME/CFS is profound, not the result of ongoing excessive exertion"*

We feel that this new name really does not convey the complexity and severity of this disorder.

In fact it retains a link to the existing perception of the disease that exists already.

The systemic disease component will be lost to many if the disease is related to exertion.

It does not move things on and is inconsistent with other observations in the report which state that fatigue is not always the main symptom experienced by patients.

As such we feel that SEID is a clumsy name which does not totally fit the objective and will be redundant in a short time once new research comes along.

There was no necessity to change the name and we feel the IOM committee have made a mistake on this point.

However, the committee clearly signals the inappropriate term CFS

> *"The term "chronic fatigue syndrome" has been the object of particular criticism from patients"*
> *"Their most common complaints are that this name is stigmatizing and trivializing, causing people not to take the disorder seriously"*

CFS is now effectively redundant.

Yet it seems a total waste of patients' lives for the authorities to allow the debate to carry on for so long around the name and do nothing to try to help find biomarkers, cause/s and treatments.

> *"In addition to difficult interactions with health care providers, patients have reported several other ways in which the stigmatization of ME/CFS affects them, including financial instability (such as job loss or demotion), social disengagement, and feeling the need to hide their symptoms in front of others "*

These difficult interactions often lead to family break ups as well as healthy family members cannot understand that someone can be so ill whilst looking fairly normal.

> *"However, ME/CFS should not be considered merely a point on the fatigue spectrum or as being simply about fatigue. Experienced clinicians and researchers, as well as patients and their supporters, have emphasized for years that this complex illness presentation entails much more than the chronic presence of fatigue. Other factors, such as orthostatic intolerance, widespread pain, unrefreshing sleep, cognitive dysfunction, and immune dysregulation, along with secondary anxiety and depression, contribute to the burden imposed by fatigue in this illness. The challenge in understanding this acquired chronic debility, unfortunately named "chronic fatigue syndrome" for more than two decades, will be to unravel those complexities."*

YES! It again makes one wonder why the need to change name now

The committee acknowledges that historically

> "*the diagnostic criteria for ME have required the presence of specific or different symptoms from those required by the diagnostic criteria for CFS; thus, a diagnosis is not equivalent to diagnosis of ME. This term fails to convey the full spectrum of this disorder*."

So we wondered if the IOM committee were proposing that SEID is meant to replace CFS, or ME, or both.

If there was a lesser extent of concern about the name ME then it should have been logical to keep that name (ME) at least until further research tells us otherwise. And by dropping CFS then the confusion about WHO coding could be avoided as ME is already classified in G93.3 in the central WHOICD10 as well as the US version ICD10CM.
ME is well established and even US researchers and clinicians have started to use ME instead of CFS in recent years.

Finally the IOM report states -

> *"many patients and researchers are critical of the term "chronic fatigue syndrome," which is the name most commonly ascribed to this disease in the United States (but not in other parts of the world). Patients in particular find this term stigmatizing and trivializing, and there is evidence to support these perspectives. The way an illness is labeled affects the illness experience (Wojcik et al., 2011). Labels convey meanings that*

affect patients' perception of their illness as well as the reactions of others, including medical personnel, family members, and colleagues (Jason and Richman, 2008; Jason et al., 2002b; Wojcik et al., 2011). As noted in Chapter 2, patients have reported that many clinicians are dismissive, making such comments as "I am fatigued all the time, too."
"Perceptions of a patient by others are important because they have been shown to affect the course of a disorder and may be associated with different outcomes."

Think about it!

"***The way an illness is labeled affects the illness experience***"

By this token the name SEID is likely to be inappropriate – it does not help patients. Despite recognising this as a disease it may not be sufficient to overcome the misinformation of the past and the term exertion does not convey the seriousness of this disease.

It is an IMPORTANT decision that the IOM report states in a conclusion of one chapter -

"***Conclusion:*** *The committee agrees that the term "chronic fatigue syndrome" often results in stigmatization and trivialization and should no longer be used as the name of this illness."*

Treatment and Name

The report validates the frustrations of patients in diagnosis and then treatment

"Diagnosing ME/CFS in the clinical setting remains a challenge. Patients often struggle with their illness for years before receiving a diagnosis, and an estimated 84 to 91 percent of patients affected by ME/CFS are not yet diagnosed
In multiple surveys, 67 to 77 percent of patients have reported that it took longer than a year to get a diagnosis, and about 29 percent have reported that it took longer than 5 years"

The report identifies the past acceptance by establishment organisations of the complete failure to diagnose properly and also the financial burden on society by these failings in treating this disease.

It also registers the cost of failure to treat ME properly -

"High societal costs of $17 to $24 billion should be reason enough to invest heavily in fundamental research to allow better understanding of the disease."

This is a point that IiME made in our response to the P2P report. The amount of money spent in dealing with the effects of this disease could be saved by following a strategy of biomedical research into ME which directly looked for the cause and pathogenesis of the disease.

The report also highlights what every patient, family and carer has known and experienced for a generation -

"Seeking and receiving a diagnosis can be a frustrating process for several reasons, including scepticism of health care providers about the serious nature of ME/CFS and the misconception that it is a psychogenic illness or even a figment of the patient's imagination.
Less than one-third of medical schools include ME/CFS-specific information in the curriculum, and only 40 percent of medical textbooks include information on the disorder.
ME/CFS often is seen as a diagnosis of exclusion, which also can lead to delays in diagnosis or to misdiagnosis of a psychological problem.

> *Once diagnosed, patients frequently complain that their health care providers do not know how to deliver appropriate care for their condition, and often subject them to treatment strategies that exacerbate their symptoms."*

Exactly! A message that IiME, and some other organisations with similar objectives, have been echoing for a decade.

A further, sobering comment underlines the apathy and negligence which has been allowed to continue for so long without any responsibility being taken -

"Literature on mortality associated with ME/CFS is sparse."

This statement is one of a number which serve as testament to the failure of the leadership in organisations such as the UK Medical Research Council (MRC) and the USA National Institutes for Health (NIH) and Centres for Disease Control (CDC) with regard to ME.

Subgrouping

As ME/CFS by any definition is a complex multisystem disease then it seems only logical to try to subgroup patients for research purposes as it is unlikely that all patients diagnosed with ME/CFS have the same disease process.

"The committee was also asked to distinguish among disease subgroups"

"The overall intent was to identify information on symptoms and objectively measurable signs (such as laboratory and imaging abnormalities) that are associated with ME/CFS and could be useful in defining ME/CFS or discriminating it- or subgroups -from other conditions."

But how can this be done if not enough known about the disease – and, as was recognised by the IOM, not enough research has been funded to achieve this?

The IOM committee was tasked "to distinguish among disease subgroups"
But due to "sparcity of research" that was not possible – further evidence of failure of establishment research funding bodies.

It was good and proper to see that the IOM committee mentioned that ME/CFS and Fibromyalgia are two distinct disorders (even though people can be affected by both).

The committee decided against developing a comprehensive list of potential comorbid conditions, but points to conditions that clinicians may wish to consider that have been identified by the ME-International Consensus Criteria (ME-ICC)

Children

The IOM report looked at the effects on children from this disease.

> *"There is clear evidence of the impact of ME/CFS on the education and social development of these young people. The stigma and social effects of pediatric ME/CFS include the loss of normal childhood activities and in some extreme instances, inappropriate forcible separation of children from their parents"*

The report acknowledges loss of normal childhood in paediatric cases and in some extreme cases, inappropriate forcible separation of children from their parents.

This is a very important point to see in writing and should help families in such difficult situations. IiME have been involved in such cases and it shames the UK social system that continues to be allowed to happen.

However, owing to flawed funding policies on research paediatric immune function studies have not been replicated.

The report mentions that further investigation of IVIG in the paediatric ME/CFS population is warranted.

> *"Given the scientific strength of the randomized controlled trial design, the larger sample size, and the reported benefit of IVIG for pediatric ME/CFS patients, further investigation of IVIG in the pediatric ME/CFS population is warranted."*

The report mentions a study that suggested a role for childhood trauma in ME/CFS used a broad empirical definition of ME/CFS, which resulted in a biased sample and overrepresentation of individuals with depression and posttraumatic stress disorder. They go on to say that "*The unusually high proportion of subjects with serious psychiatric problems likely explains the study finding of an association between ME/CFS and adverse childhood experiences."*

This is good to see in print for use in situations where families need to explain themselves to authorities who may have taken this study by Heim et al., 2009 at face value. There have been references to this study in the media and elsewhere in connection of children with ME/CFS and it is now useful to see this study needs to be completely dismissed as flawed research. **It is also good to put this old chestnut of childhood trauma to bed for good**.

The IOM recognise the impact on education from this disease.
Among 25 children recruited from a UK support group only 1 attended regular classes.
Of 211 children referred to a specialist clinic in England, 62 percent attended school 2 days a week or less.

The isolation for children affected by this disease in school years is a major factor which society needs to address and schools need to be criticised for their lack of knowledge of the disease and their apathy to attempting to keep children linked in some way to their school class. This is not difficult to do and can have a helpful effect on a child's longer term health.

The most prevalent pain symptom in children was headache, reported by 75 to 81 percent of patients in a number of studies – an interesting observation when one considers the earlier suggestion of a name change.

Australian study of 189 adolescents by Rowe and Rowe concluded that evidence for somatization disorder among young people with ME/CFS was negligible.

> *"They all note that ME/CFS symptoms often make it more difficult to do schoolwork, so children and adolescents with ME/CFS may be misclassified as having "school phobia."*

IiME deplore the concocted term **school phobia**, and those promoting it in relation to ME/CFS, which has never applied to children with this disease.

The committee stated that it is important that children are given an early 'CFS' like diagnosis within 1-2 months before any definite diagnosis can be made to help alleviate any worsening of their condition by unhelpful treatment and advice.
6 months duration of symptoms for the diagnosis of ME/CFS in children. The committee emphasizes that the time criterion should not interfere with initiating appropriate symptom-based management long before 6 months has elapsed and whilst the process continues to evaluate and exclude other conditions.

Again the mediocrity in leadership of MRC/NIH regarding research into ME/CFS is referred to as it was recognised that there was little research in paediatric studies.

ICD

We are glad to see [Recommendation Number 1] that a thorough history, physical examination, and targeted work-up are recommended for diagnosis and this obviously takes place before a six month cut off point.

In recommendation Number 1 the IOM also states that ME

> *"A new code should be assigned to this disorder in the International Classification of Diseases, Tenth Edition (ICD-10), that is not linked to "chronic fatigue" or "neurasthenia."*

The WHO Tenth Revision this document refers to is the US ICD10CM version.
The US WHO ICD10CM does not control what the central WHO decide and the central WHO have so far said there is no plan to change the classification of ME away from G93.3.

We therefore find this inconsistent and confusing.

We feel that the classification should be kept at G93.3 - as it is in the European WHO ICD10.

The central WHO ICD10 codes Postviral Fatigue Syndrome and benign myalgic encephalomyelitis at G93.3 and CFS is linked to the same code via the index.

We feel that ME/CFS is such a multisystem illness that symptoms from almost any other condition may overlap so it should not be helpful to diagnose a comorbid condition unless the criteria for that co morbid condition are clearly met. It is not helpful for patients to blend in too many conditions into one, certainly not for research purposes.

Careful phenotyping is useful for the right kind of treatment to be administered for each patient.

Establishment Research Councils and Research Strategy

The IOM report accurately reports on the current pitiful state of research into ME/CFS, the method by which research is carried out and the funding decisions made toward research in to ME/CFS.

The lack of consistency in research criteria, the flawed policy of funding psychiatric theories and the failure to even standardise on methods and terminology are all shown to contribute to the mess that has been ME/CFS research.

The following statements from the IOM report again highlight the culpability of those establishment organisations responsible for research funding for ME -

- *"the committee was struck by the relative paucity of research on ME/CFS conducted to date. Remarkably little research funding has been made available to study the etiology, pathophysiology, and effective treatment of this disease, especially given the number of people afflicted. Thus, the committee was unable to define subgroups of patients or even to clearly define the natural history of the disease. More research is essential."*

- ***"**When evaluating the available research to develop its findings, conclusions, and recommendations on pediatric ME/CFS, the committee was struck by the paucity of the research conducted to date in this population.**"***

- *"Almost all the studies conducted to date have compared patients with ME/CFS with healthy controls rather than with patients with these other fatiguing disorders."*

- *"One of the most significant challenges to achieving a better understanding of ME/CFS results from the methodological limitations of the current research base. Issues related to external and internal validity and to reliability frequently have led to inconsistent results across studies, as well as other shortcomings"*

- *"As with other literature on ME/CFS, the use of different diagnostic criteria for patient selection limits comparisons across studies. In particular, because of the variations in diagnostic criteria for ME/CFS, some studies excluded patients with primary sleep disorders, while others included them"*

- *"Studies on ME/CFS used different inclusion criteria and different sources of ME/CFS patients and control participants. The end result is het-erogeneity in both patient and control cohorts, creating an unclear picture of the symptoms and signs of the disorder and its outcomes. Findings are based on samples with a large majority of middle-aged women (late 40s to early 50s) who are Caucasian and of higher educational status, perhaps limiting the generalizability of the studies. Very few studies focused on other population subsets, such as pediatric or geriatric patients, or included ethnic and racial minority patients. Some studies recruited patients from specialized ME/CFS treatment centers, while others used community-based samples.* ***These different sampling methods may result in patient groups that differ in demographic characteristics and symptom type and severity***.
  Furthermore, those most severely affected by ME/CFS may be bedridden or homebound and may not have been included in any of these studies (our bold type)
  Thus, there are selection biases in the studies' sample composition."

The countless times that it is stated that research used inconsistent criteria or significant variations in research ("*because of the methodological weaknesses in much ME/CFS research*") underlines what a mess research has been over the last decade/15 years – and it is funding bodies such as the MRC/NIH who have to take full responsibility.

These are all damning indictments of MRC and NIH policies, and of those leading these organisations over the last decade. Research strategy from organisations such as these, using public funds, has been truly pathetic.

Those who were and are responsible for managing the various committees or panels need to be singled out for major criticism.
Those currently still in positions where they had any responsibility for any part of the past 10 years of policies should have the honour and integrity to review their roles in allowing this mess to continue for so long.

We have pointed out that the decisions and efforts by these people have directly affected lives of people with ME and their families.

How many lives have been affected, wasted by the policies and decisions of these people and their associates?

> *"Despite Dr. Ramsay's work and a U.K. independent report recognizing that ME is not a psychological entity (CFS/ME Working Group, 2002), the health care community generally still doubts the existence or seriousness of this disease. This perception may partly explain the relatively limited research efforts to study ME in fields other than psychiatry and psychology."*

We agree – but it is also thanks to the policies of the UK MRC and USA NIH/CDC which has allowed this false view to be maintained.

Without a total abrogation of responsibility from these organisations, especially those leading the policy on ME/CFS, the perception mentioned by the IOM report would not have been allowed to remain.

The IOM report states -

> *"Finding the cause of and cure for ME/CFS may require research that enlists large numbers of patients with this disorder from which important subsets can be identified in terms of disease symptomatology, responses*

> *to physical and cognitive stressors, brain imaging, the microbiome, virology, immune function, and gene expression. Integrative approaches using systems biology may be useful in unraveling illness triggers. Studies aimed at assessing the natural history of the disease and its temporal characteristics (onset, duration, severity, recovery, and functional deficits) are essential for a better understanding of ME/CFS."*

All these are good points being made and hopefully funding will now be made available for researchers who want to pursue these tasks.

There is no lack of interested researchers if they know there is consistent funding available.
IiME have proven this in our attempts at establishing our annual research colloquium in London which has, for more than five years now, attempted to bring in researchers from other disciplines and crowdfund to enable proper research strategy to be formed.

The IiME research colloquiums [9] over the years have come to the same conclusion that there are and have always been enough clues to further invest in ME/CFS research.

Unfortunately there has been very little interest from the public bodies in supporting fundamental research in this area and ME/CFS is therefore far behind other diseases and deserves major attention to rectify past mistakes and neglect.
The report also states that pediatric immune function studies have not been replicated.

Lack of replication and validation is a major problem and it is good to see it acknowledged here.

> *"It is encouraging to note that progress already is being made in understanding the etiology, natural history, pathophysiology, and effective treatment of ME/CFS using a variety of physiological and molecular methods.*
>
> *Several large cohort studies are now under way. The committee expects that this research will lead to findings that can be used to further refine the diagnosis of this disorder and the elaboration of clinically pertinent subtypes.*
>
> *As a result, the committee calls for a reevaluation of the evidence in no more than 5 years using the methods recommended in the IOM report Clinical Practice Guidelines We Can Trust (IOM, 2011)."*

Much of the above is inherent in IiME's strategy toward research and we agree with the points mentioned.

It is good that it is pointed out that choosing from a wide list of neurological impairments does not guarantee to choose patients that have the same disease process and therefore it is all the more important to try to phenotype patients for research and treatment purposes.

It is important to have research that can tease out subgroups as it is may be unlikely that all ME, CFS or ME/CFS patients are the same no matter which diagnostic criteria are being used.

The report does show up the inconsistencies in research – from different diagnostic criteria used to define cohorts to different interpretations of symptoms, such as fatigue. This again points to a lack of leadership in research councils responsible for funding. There has been no joined-up thinking.

> *"Most authors identify fatigue-type factors as an integral symptom construct of ME/CFS.*
> *In two studies, fatigue is considered part of a multidimensional construct encompassing fatigue, mood, and cognition, while in two other studies, fatigue is considered part of a bidimensional construct related to either rest or PEM.*
> *Several studies identify a "neurocognitive difficulty" factor that includes such symptoms as slowness of thought; mental fog; and problems with concentrating, memory, or understanding.*

Some identify a "musculoskeletal" factor that includes such symptoms as muscle or joint aches and pains and weakness;
a "viral flu-like" factor that includes such complaints as fever, sore throat, and tender lymph nodes;
an emotional distress or mood or anxiety disturbance factor;
a somatic factor that includes such gastrointestinal complaints as stomach pain or diarrhea;
and a sleep difficulties factor)"

Also

"It is clear, however, that people with ME/CFS universally report experiencing unrefreshing sleep, and further research will be important to determine whether there is a specific sleep abnormality common to ME/CFS patients or a heterogeneity of abnormalities that may define subsets of ME/CFS patients."

This is all the more reason to invest in some serious biomedical research into this disease, research that can find molecular markers to stratify patients and use responses to clinical trials as a means to understand the pathomechanism and subgroups.

"it is important to consider symptom thresholds that take severity into account when operationalizing any diagnostic criteria for ME/CFS."

It is correct and good that the limitations of using different criteria to choose patients are identified. One needs long term follow up studies and epidemiological studies that use community samples to see the real extent of this disease.
It is also correct and appropriate to recognise that "***those most severely affected by ME/CFS may be bedridden or homebound and may not have been included in any of these studies***"

The IOM report recognizes the lack of research into the early stages of the illness even though a firm diagnosis is not made until after 6 months.
Epidemiological studies that would collect long term data would be helpful in understanding the dynamics of the disease.
The length it takes to diagnose has been discussed often at IiME research meetings/conferences and it is a double edged sword as some clinicians say that they have had patients that had for example contracted an ME/CFS like illness having travelled abroad but recovered after 12 months or so.

The IOM report discussed brain studies

"While in general these studies have been small (most with fewer than 20 patients with ME/CFS, usually fulfilling the Fukuda definition), most have shown statistically significant differences between patients with the condition and controls using a wide range of technologies and in a variety of brain regions. "

Varying locations of the findings make insight into aetiology and treatments less clear, and subsets of patients have not yet been defined.

*"**Summary***
Collectively, the studies reviewed here support the notion that ME/CFS patients present with neurocognitive impairment. Slowed information processing, demonstrated by objective neuropsychological testing and potentially related to problems with white matter integrity, is one of the strongest neurocognitive indicators in support of a diagnosis of ME/CFS, particularly if there is evidence of normal functioning on untimed tests and impaired functioning on time-dependent tasks.
*The greater severity of memory and other neurocognitive deficits in ME/CFS patients without psychiatric comorbidity suggests that **these deficits may be a distinguishing feature of the disease,** or at the very least a means of defining subgroups within the ME/CFS population. Confirming the presence of this symptom using objective neuropsychological testing would support diagnosis of ME/CFS and possibly support diagnosis of a specific subset of ME/CFS patients, but is not necessary for the diagnosis."*

The report states conclusively that there is sufficient evidence for immune dysfunction in ME/CFS.

It states that there is "*insufficient evidence to conclude that any specific neuroendocrine abnormalities cause ME/CFS."*

It states that there is sufficient evidence suggesting that ME/CFS follows infection with EBV and possibly other specific infections.

Enteroviruses are discussed but the report states there is no evidence strong enough to support this

Subtyping was encouraged for researcher-determined characteristics such as length of illness, infectious onset or objective test results such as treadmill testing, immunologic markers. Researchers and clinicians agree that ME/CFS is a heterogeneous condition

"It is essential that clinicians assess the severity and duration of symptoms over an extended period of time because moderate or greater frequency and severity of symptoms are required to distinguish ME/CFS from other illnesses."

The report mentions the need for a set of distinctive biomarkers as a priority. We could not agree more and hope to see much more funding invested in such fundamental research.

It is good to see mentioned that the committee was struck by the paucity of research on ME conducted to date in many areas. They said that remarkably little research funding had been made available to study the etiology, pathophysiology, and effective treatment of this disease, especially given the number affected.

We hope our recommendation from our P2P report is taken seriously and much more funding is invested in fundamental ME research. There are researchers interested in studying this disease - they just need assurances that funding is made available, hopefully ring fenced so that ME/CFS patients can catch up with other diseases.

Patients need to be compared with other neurological illnesses too and not just fatiguing disorders.

Severely ill patients also need to be researched and their condition should be compared to other severely ill bed bound patients such as bed bound stroke victims, cancer patients etc.

Severely ill ME/CFS patients may be a heterogeneous group too and until they are included in research efforts we may never know what exactly it is that leads to or maintains their severe form of ME/CFS.

Calls for homogeneous sample of patients from which important subsets can be identified in terms of disease symptomatology, responses to physical and cognitive stressors, brain imaging, the microbiome, virology, immune function, and gene expression. Integrative approaches using systems biology and studies aiming at assessing the natural history of the disease are also mentioned.

We concur with the IOM report – "***More research is essential."***

We wait to see words put into action.

International

"This report had domestic (US) focus but major international issues may be identified. As the research into ME/CFS is so sparse it would help if the international medical/research community agreed upon the disease and the way it needs to be researched so that no more lives are being wasted due to constant inconclusive research results that lead nowhere."

We agree with this statement. It underlines and embodies all that IiME have attempted to achieve in the last 10 years. A welcome justification of the strategy of those independent organisations who have been trying to change things away from establishment status quo of doing and funding as little as possible.

Welfare

> *"Seeking and receiving a diagnosis can be a frustrating process for several reasons, including scepticism of health care providers about the serious nature of ME/CFS and the misconception that it is a psychogenic illness or even a figment of the patient's imagination."*

Indeed. The policies of establishment organisations funding research have been partly responsible for this.

A useful comment that should aid patients in dealing with the ideologically-driven government policies aimed at targeting disabled people (as has occurred in recent times in UK) is this -

> *"Symptoms can be severe enough to preclude patients from completing everyday tasks, and 25-29 percent of patients report being house- or bedbound by their symptoms. Many patients feel unable to meet their family responsibilities and report having to reduce their social activities (NIH, 2011). However, these data include only patients who were counted in clinics or research studies, and may underrepresent the extent of the problem by excluding those who are undiagnosed or unable to access health care"*

> *"Many patients report barriers to accessing health care as well, including the nature of their illness and financial considerations"*

This is a direct consequence of the lack of knowledgeable doctors who can diagnose and treat these patients in the same way they do other chronically ill patients.

Some patients, especially the severely ill ones in the UK, rarely see a doctor.

Families with children prefer to keep a low profile due to fear of court action if the children fail to improve on the usual CBT and GET/GAT activities advocated by the NICE guidelines.

It is good to see the impact on work and education mentioned. The charity's experience is that very few people manage to stay at work even at reduced hours and children mostly miss school completely and at best can manage a few hours of home education per week. It is simply not possible for children to try to attend normal classes when ill as the environment is far too busy and noisy.

Another useful statement -

> *"Patients with ME/CFS have been found to be more functionally impaired than those with other disabling illnesses, including type 2 diabetes mellitus, congestive heart failure, hypertension, depression, multiple sclerosis, and end-stage renal disease"*

US Social Security Ruling 2014 is based on adaptations of the Fukuda definition and some elements of the CCC and ME-ICC.

> ***"Conclusion:** There is sufficient evidence that fatigue in ME/CFS is profound, not the result of ongoing excessive exertion, and not substantially alleviated by rest. This fatigue results in a substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities and persists for more than 6 months."*

Memory impairment does appear to distinguish ME/CFS from depression and anxiety but less clear in distinguishing it from other fatiguing illnesses.

> *"Cognition has been found to be weaker among patients with ME/CFS, with impaired ability to maintain attention and alertness"*

Laboratory evidence of prior infection is not required to diagnose this disorder but it may be needed for other reasons, such as obtaining Social Security Disability; the presence of virus specific immunoglobulin M (IgM), if documented near onset of illness, may support diagnosis.

The IOM report recognised that most patients never regain their premorbid level of health or functioning.

> *"Symptoms can persist for years, and most patients never regain their premorbid level of health or functioning"*

P2P Considerations

IiME commented on the P2P report [2] and one would have expected the P2P and IOM to cooperate or share data and experience – if only to be more efficient, consistent and accurate. We found this statement in the IOM report remarkable -

> *"The study's statement of task also directed the committee to seek input from NIH's Evidence-based Methodology Workshop for ME/CFS, a process now referred to as Pathways to Prevention (P2P). The NIH P2P workshop was originally intended to complement the present study by developing a research case definition for ME/CFS (CFSAC, 2012). However, in remarks on behalf of the P2P workshop process at the committee's first public session, Susan Maier, Deputy Director for NIH's Office of Research on Women's Health, stated that the goal of the P2P workshop was not to develop a research case definition but to suggest a research agenda for ME/CFS based on an unbiased review of the evidence. She also expressed a desire to work with this committee throughout the P2P process.* ***However, the planning group for the P2P workshop declined to share any data with the committee.****"*

> *"The NIH P2P workshop was originally intended to complement the present study by developing a research case definition for ME/CFS (CFSAC, 2012). However, in remarks on behalf of the P2P workshop process at the committee's first public session, Susan Maier, Deputy Director for NIH's Office of Research on Women's Health, stated that the goal of the P2P workshop was not to develop a research case definition but to suggest a research agenda for ME/CFS based on an unbiased review of the evidence."*

This is Incredible.

This shows a level of waste involved in this process. The P2P was originally instructed to develop a research definition but this was later changed to a task to suggest a research agenda into ME/CFS. The IOM was to create a clinical definition. Why weren't these initiatives joined up? It seems odd that the NIH funded P2P workshop process tasked to develop a research agenda has not shared any data with the IOM committee.
This is a tragic and unnecessary waste of resources and opportunity.

Surely it would benefit patients if these two projects had shared data to avoid any contradictions?

Already we can see one such contradiction in that the IOM has renamed ME/CFS as Systemic Exertion Intolerance Disease yet the P2P draft report states that cognitive behavioural therapy (CBT) and graded exercise therapy (GET) demonstrate measurable improvement and should be used as a component of multimodal therapy.

This is inconsistent and potentially damaging.

Providing two different messages from influential reporting bodies undermines confidence in both and serves no good for patients who remain at the end of currently deleterious processes from healthcare organisations and individuals and from the results of poor research funding decisions.

For the record, on this particular point, we side with the IOM report – there is nothing to support the idea of efficacy of CBT or GET as treatments for ME/CFS.

The IOM report looks to be a good review based on really looking at the issues – and removes the disingenuous comments of psychiatrists based in the UK over a generation who have denied this illness.

As we stated in our P2P submission – funding is key.

Some of the use of inconsistent criteria may be historical – the chronology of criteria means that results are dependent on when the research was performed. But CCC have been available for over ten years.

The P2P report has stated clearly how meaningless the Oxford criteria are known to be for ME/CFS research. All research using those criteria should be discarded as reference for ME/CFS.

IOM Recommendations

The IOM had the following recommendations –

Recommendation 1:

> **Physicians should diagnose myalgic encephalomyelitis/chronic fatigue syndrome if diagnostic criteria are met following an appropriate history, physical examination, and medical work-up. A new code should be assigned to this disorder in the *International Classification of Diseases*, Tenth Edition (ICD-10), that is not linked to "chronic fatigue" or "neurasthenia."**

We agree with the first point in the above recommendation.

We disagree with the need at this time for another ICD classification code as one already exists and is agreed internationally. That code is ICD-10 G93.3 Myalgic Encephalomyelitis/Post Viral Fatigue Syndrome.

When the committee also recommends that "more complex tests that may be helpful in cases of diagnostic uncertainty or long-term management" we wonder who will pay for this. We therefore believe the committee should specifically state that healthcare systems must fund these extra tests.

Recommendation 2:

> **The Department of Health and Human Services should develop a toolkit appropriate for screening and diagnosing patients with myalgic encephalomyelitis/chronic fatigue syndrome in a wide array of clinical settings that commonly encounter these patients, including primary care practices, emergency departments, mental/behavioral health clinics, physical/occupational therapy units, and medical subspecialty services (e.g., rheumatology, infectious diseases, neurology).**

This is important and the method of distribution/dissemination/implementation will determine the success of this.

Recommendation 3:

> **A multidisciplinary group should re-examine the diagnostic criteria set forth in this report when firm evidence supports modification to improve the identification or care of affected individuals. Such a group should consider, in no more than 5 years, whether modification of the criteria is necessary. Funding for this update effort should be provided by nonconflicted sources, such as the Agency for Healthcare Research and Quality, through its Evidence-based Practice Centers process, and foundations.**

> ***Conclusion:*** *The committee agrees that the term "chronic fatigue syndrome" can result in stigmatization and trivialization and should no longer be used as the name of this illness.*

We agree that the diagnostic criteria, whichever are used, need to be revisited on a regular basis using results from new research. But we also feel this will matter little if enough research funding is not made available to carry out a strategy of biomedical research into ME. The recommendations from our P2P report need to be carried out.

Recommendation 4:

> **The committee recommends that this disorder be renamed "systemic exertion intolerance disease" (SEID). SEID should replace myalgic encephalomyelitis/chronic fatigue syndrome for patients who meet the criteria set forth in this report.**

SEID is a clumsy term and still implies fatigue. This is not the only prime feature and the name will need to be reviewed already in a short time.

"The committee intends for this name to convey the complexity and severity of this disorder"

We do not feel it does this. The committee stated previously that there is paucity of research so we wonder of the wisdom of trying to change the name at this point.

It does not future-proof the term or the way the disease is treated – it means that it remains in a doubtful status where patients remain dissatisfied, researchers unable to guarantee a future involved with this and still open to public conception – or worse by more puerile media and public simplistic assumptions.

However, now stating this is a disease and systemic is a good way forward. It is just a pity that it was not better analysed.

IIME SUMMARY

The IOM concludes with what patients have been fighting to make known for a generation – to governments, research councils, health services, the media and the public

> ***"Conclusion:** It is clear from the evidence compiled by the committee that ME/CFS is a serious, chronic, complex, multisystem disease that frequently and dramatically limits the activities of affected patients."*

We summarise below the points from the report that we feel are worth noting

- IOM is a respected and influential institute
  This means that the good points from this report can be quoted elsewhere to aid convincing other healthcare authorities that ME needs to be treated seriously as a systemic disease.
- IOM did an extensive literature review
  This means that the good points from this report can be quoted elsewhere to aid convincing other
- The proposed new diagnostic criteria are clinical criteria for the US healthcare system
- There was only one European and no UK reviewers involved so it remains to be seen whether the UK and other European health care authorities will adopt this report
- The criteria allow co-morbidities which seems sensible for clinical purposes as anyone can have more than one disease.
- Care should be taken to avoid misdiagnoses and this is why specialists are needed to oversee diagnosis
- Researchers use stricter criteria based on the requirements of their projects and they may sometimes choose cohorts with or without comorbidities. This would be no different from research into any other disease.
- PEM is obligatory not optional for diagnosis and this is the one defining symptom that patients say was missing from CDC Fukuda
- Both the IOM report and the P2P draft report call for more research and highlight the serious lack of research into this area of medicine compared to the numbers of patients involved
  "Literature on mortality associated with ME/CFS is sparse."
  Also subgrouping was a task to be analysed by the IOM committee but due to the sparcity of research that was not possible.
- The implicit result of the above commentary is a direct condemnation of the research and funding policies of the UK Medical Research Council and US National Institute for Health
- This report is essentially far better than the UK CFS/ME NICE guidelines which were heavily biased toward CBT and GET and did not encourage, for example, further investigation into the promising IVIG paediatric research (Rowe, 1997) which the IOM does
- It is good that the committee declares that ME/CFS is a physical illness, a disease
- The IOM definition and the name goes against treatments such as CBT and GET and contradicts the P2P report in that respect.
- The report states that ME/CFS is a diagnosis to be made and provides good suggestions for asking questions and eliciting medical history as well as assessing supportive symptoms such as sleep disturbance and pain.

  There needs to be extensive medical education to make more doctors confident in making the diagnosis but we need centres of excellence and experienced consultants to oversee the education.
  Diagnosing patients according to them fitting in the diagnostic criteria rather than by exclusion of other illnesses is good.

  One of the committee's most important conclusions is that a thorough history, physical examination, and targeted work-up are necessary and often sufficient for diagnosis of ME/CFS.

  This point has often been emphasized by clinicians speaking at IiME conferences too. It is also all the more important to invest in fundamental research that can come up with objective and easily implemented tools for aiding diagnostic accuracy.
  "First and foremost, listening to patients and taking a careful history are key diagnostic tools."

- It is good to see mentioned that even if patients do not meet the criteria for this disease, clinicians should address their symptoms and concerns. Patients who have not yet been symptomatic for 6 months should be followed over time to see whether they meet criteria for ME/CFS at a later time.
- The report mentions objective tests such as CPET or tilt test being useful for gaining social security but not necessary for diagnosis due to risk for worsening the patient's condition
- The report calls for research into biomarkers and acknowledged there being sufficient evidence for immune dysfunction despite there not being reliable markers for clinical use yet
- The report recognises that most patients never regain their pre-illness levels of health or functioning
- The report recognises inappropriate removal of children from their families in some extreme cases – though perhaps more common in the backward UK environment
- The report rejects childhood trauma and somatisation as being part of paediatric cases
- The IOM recognise the impact on education from this disease for children. The isolation for children affected by this disease in school years is a major factor which society needs to address and schools need to be criticised for their lack of knowledge of the disease and their apathy in attempting to keep children linked in some way to their school class.
- The report recognises impact on employment and education
- There was no public consultation as happened in the P2P or UK NICE guidelines
- The report stated that CFS is not appropriate. This aligns with the P2P report

  The committee determined that the name “chronic fatigue syndrome” has done a disservice to many patients
- It was not totally clear if the recommendation for a name change was to replace CFS or ME or both.

  The report rejected the long established name myalgic encephalomyelitis (ME) stating there not being enough evidence to justify the correctness of the name and that the name “myalgic encephalomyelitis” does not accurately describe the major features of the disease.

  Yet, even if one believed that to be correct, it seems to ignore the fact that there are other diseases with incorrect names such as malaria and hay fever and they have not been changed. The UK MRC states that there is now evidence of neuroinflammation in some severe cases of ME. This is no different from for example of poliomyelitis where the mild cases may appear unremarkable and go even unnoticed.
- In place of ME the committee proposes SEID “systemic exertion intolerance disease” as a name that more fully captures the full scope of this disorder.

  We feel this is not a progressive decision and provides a name not so dissimilar from the ineffectual and inappropriate CFS

  Both the P2P report and the IOM report fail to move away from the association of ME with fatigue as the main symptom. That ought to have been addressed. They should have recommended dropping CFS and used ME until more is known as ME is well established in the name and even US researchers and clinicians have started to use ME instead of CFS in recent years.
- SEID is a clumsy acronym and many people seem to type SIED already but it is better than CFS.

  Although better than CFS, and confirming this is a systemic disease, the use of a potentially misunderstood fatigue-associated word means that this will be bound to retain the implication of ME/CFS being a fatigue illness
- Systemic and Disease are easy to accept but Exertion Intolerance will not be well understood by the general public and will be confused with exercise (physical) intolerance only.
- The US WHO ICD10CM does not control what the central WHO decide and the central WHO have so far said there is no plan to change the classification of ME away from G93.3
- SEID is said to replace CFS (US WHO ICD10CM code R53.82 which includes CFS not otherwise specified (CFS NOS) but excludes post viral fatigue syndrome (PVFS) which has the same code as benign myalgic encephalomyelitis G93.3 so ME and PVFS would presumably stay as they are even in the US WHO CM codes
- The criteria are more specific than the CDC Fukuda but wider than CCC or ICC. This may lead to an influx of patients for the few US specialists. Is that the intent? Or is there a plan to train more specialists?
- Is there sufficient infrastructure in place to deal with the large percentage of undiagnosed patients that this report refers to?

- Who takes responsibility for the follow up work or will this expensive report end up like the UK CMO, 2003 report whose recommendations were not acted upon?
- Does anyone currently diagnose ME in the US? If so, which criteria do they use?
- If CFS and ME have traditionally had different criteria as stated in the report and the IOM report used ME/CFS as in the CCC then it was somewhat unclear whether this report meant to combine the two definitions into one
- The P2P draft report calls for agreement on one set of criteria but the IOM report has created criteria for SEID to replace CFS and recommends classification away from fatigue codes (we assume they refer to R53.82 CFS NOS and not ME and PVFS which are already in the neurological code of G93.3)
- Most ME, CFS or ME/CFS research has been performed using the CDC criteria and more recently the CCC or the combination of CDC and CCC and hardly any research has been performed using the ICC or the Ramsay Criteria. The ICC is based on research that has used CCC or CDC criteria. This just goes on to show that researchers use various criteria and then it is used as evidence for any of the acronyms of CFS, ME/CFS or ME depending on the users and it would be sensible to use criteria that are inclusive for diagnosis but allows for specific phenotypes to be selected for research.
- The IOM panel included ICC signatories Drs Lucinda Bateman and Nancy Klimas. The ICC 2011 states that the panel recommended the use of myalgic encephalomyelitis for patients who meet the ICC criteria because a distinctive disease entity should have one name. So does this mean that the ICC should be used for ME and the IOM report for SEID?
- Less than one-third of medical schools include ME/CFS-specific information in the curriculum
- For years ME and CFS patients have been let down by the disbelieving medical profession and hopefully this report benefits patients rather than cause yet more problems
- The few doctors/researchers that have believed in patients have been let down by their colleagues and research funding bodies and we hope that the HHS and NIH now take ME and SEID seriously and allocate funding based on them being physical diseases
- The report acknowledges high societal costs and recommends that the guidelines are revisited in no more than five years to allow new research findings to be taken into account

> *"Ideally, experienced individuals without significant conflicts of interest should conduct a systematic literature review to address the key questions."*
>
> *"Members of this group should clearly disclose their potential conflicts of interest, and the conveners of the group should try to limit the number of members with significant conflicts, who should in no case represent a majority of the group's membership."*
>
> *"There is no adequate evidence to enable comment on the manifestations of ME/CFS across the life course."*
>
> This is an acknowledgement which NICE and the MRC have never made in the UK where vested interests continue to affect what is funded or reported.

In Conclusion - Going Forward

As the report admits *"Patients, advocates, researchers, and clinicians expressed strong opposition to the study, arguing that the IOM lacks the expertise to develop clinical case definitions"*

Yet as the IOM insisted on continuing this exercise then they set up a unique opportunity to make things better.

Will this report promote the prompt diagnosis of patients with this complex, multisystem, and often devastating disorder; enhance public understanding; and provide a firm foundation for future improvements in diagnosis and treatment?

After so long a period where governments, medical research councils, health departments and some of those supporting organisations have completely abrogated their responsibilities to patients with this disease then it might be too optimistic to expect one report to overturn all that has been allowed to be wrong with the research into, perception and treatment of ME.

But a start has to be made.

In the absence of anything else one must take what one can and build upon it. And there are many good points in the report.

If the intent to improve the situation for people with ME and their families is honest then elements from this and the P2P report can change the way healthcare professionals treat the disease.

The good points from this report ought to force and demand a radical rethink of Health Institutes' and Research Councils' policies – something long overdue.

To exact a greater morality amongst research funders might be one benefit from this.

Name

Unfortunately, however many good points there may be in this report the name will be something which many will interpret and then relate to their perception of the disease.

We believe the suggested name is ill thought-out and needs to be rethought.
Whilst it is obviously logical and correct to remove the term CFS and Chronic Fatigue we feel it is not a sensible strategy to change the name to the suggested SEID at this point.
Even if the intent was honourable the name will still influence how this disease is treated.
Just as with food the contents in the tin may be completely ignored due to poor labelling.
By deciding to tinker with the name of this disease one is also obliged to examine the history and politics behind it and understand why such a name change could offend, discriminate, confound, disappoint or just enrage some patients.

Playing with the name and using exertion – however the correctness in medicine may be different from lay perception – will still invoke an initial response of this is being a fatigue illness rather than a systemic disease.

So we suggest retaining Myalgic Encephalomyelitis (ME) until enough current data is found to support or otherwise. ME (itis) is already in the WHO, it does not stop research, it removes the rather useless CFS denigration and still allows a correct view to be presented.

Criteria

Whilst it may be good that a set of simplified criteria are produced there is the concern that the criteria listed by the IOM report may be too broad. The criteria also need to be validated first to see if they really capture the right kind of patients. At the Invest in ME conferences there have been calls for the need for simple diagnostic criteria.

However, the committee also added a table with many more symptoms which could be used to support the diagnosis.

It will require education of doctors to make them able to identify the disease and avoid incorporating misdiagnoses into the assessment. The multiple comments within the IOM report relating to lack of belief from healthcare staff are evidence that this education is important.

Distribution

An obvious point – but one which needs reaffirming for any diagnostic criteria used -

> *"The criteria proposed here will not improve the diagnosis and care of patients unless health care providers use them"*

Apart from the name the distribution of the other sensible points from the IOM report needs to be managed, monitored and followed-up in order that uptake of ME being a real systemic disease in ensured.

In the UK the CMO report of 2002 [10] produced seven recommendations. It would be a disaster if the IOM report ended up like the CMO report in the UK where none of the recommendations were implemented and the psychiatric lobby who refused to sign the report went on take charge of the fatigue clinics and obtained all of the public research funding.
At that time the participating psychiatrists should have been left out. But what has transpired is that they have still been allowed to control the debate in the UK.
We would urge the US authorities to avoid a repeat of that.

The report makes a major point -

> *"Key to this effort will be the continued positioning of ME/CFS as a legitimate disease that occurs in both children and adults and should be properly diagnosed and treated."*

What can be very helpful is if the information emphasises ME/CFS as a serious physical illness and that in itself leads to health care providers taking a correct attitude toward these patients despite there being no cure or effective treatment being available yet. Just informing patients to avoid overexertion in the early stages of the disease can make a huge difference in the outcome of the disease.

It is good that the committee recommends continuing surveillance of the evidence and revisiting the criteria in no more than five years. But if

> "*The committee recognizes that new and accumulating evidence will likely enable refinement of the diagnostic criteria proposed in this report and possibly define subtypes of the disease or even distinct entities*"

then this would also mean that the name SEID would have to be revisited and almost certainly changed.

The toolkit for screening and diagnosis is an important part of the process. If this is not done properly then it is no good of having all of these recommendations.
Again, there is a need for centres of excellence such as IiME have proposed [11] and experienced clinicians that can oversee this work.

Research

The report has underlined a core message from the earlier P2P report – namely how mediocre has been the research to date on such a serious disease;

The report is a major indictment of negligent MRC/NIH/CDC policy, highlighting the way that research and treatment and information about ME have been totally misrepresented over the last generation by false funding policies, flawed research and vested interests.

What a waste of life has been allowed to occur by governments from their failure to monitor progress or listen to continuing and mounting patient concerns; how corrupt and immoral has been the attitude of those leading the organisations which use public funding of ME research, given mainly to researchers who consider ME/CFS a psychosomatic illness?

Our overriding feeling is that the report highlights the complete lack of any strategy to research this disease properly by those entrusted with the responsibility to do just that.

The aim now should be to find a speciality that owns ME/CFS or make ME/CFS a speciality in its own right – and this will not be psychiatry.

The onus is on the IOM and P2P to honour those good points from these reports – and to translate these into action.

Clearly a dramatic and immediate increase in funding for biomedical research needs to be made. IiME suggested $250 million dollars for the next five years. This problem needs to be fixed so the clear message from IiME to NIH and IOM is – FIX IT!

This will be a long haul. Those in NIH and CDC – as well as those in UK MRC - and the respective government health ministers who have been responsible for ME research and funding and guidelines over the last generation have been incompetent, or worse. So lessons have to be learned from these past failures to ensure the same fatal mistakes are not made again.

As we ended our P2P report evaluation - Words are fine and Progress is a fine word – but change is its motivator – and it is action that delivers change

These organisations and those leading them will be judged by their actions.

The task now is to implement the good points of this new acceptance of ME as being the real disease that patients already know it is.

To restate the opening remarks in the IOM report, -

> ***"Knowing is not enough; we must apply.***
> ***Willing is not enough; we must do."***
> —Goethe

References:

1	Institute of Medicine (IOM) entitled "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness"
2	Invest in ME UEA/IFR gut micriobiota study
3	Invest in ME UK clinical trial of rituximab
4	http://www.investinme.org/IIME%20Statement%202013-11-01.htm
5	P2P report
6	Invest in ME Response to P2P report
7	Rituximab trials in Norway
8	MRC accepts evidence of neuro inflammation in some severe cases of ME
9	The IiME research colloquiums
10	UK CMO report of 2002
11	IiME proposal for a UK Centre of Excellence for ME