

Position Statement on ME/CFS Criteria

Recent government actions, patient advocacy efforts and an ME/CFS experts' letter have brought attention to a very important issue: the need for more accurate and widely used ME/CFS disease criteria.

As events unfolded in recent weeks, we have been contacting Chronic Fatigue Syndrome Advisory Committee members, Gulf War illness advocates, ME/CFS researchers, members of the International Association of CFS/ME and other patient advocates. We wanted to make sure we take action that is based on accurate knowledge and not assumptions. In these conversations, we sought to get more details on what is being done and what is planned, and we expressed our concerns to all these parties of what we feel is in the best interests of ME/CFS patients, most of whom do not have access to knowledgeable healthcare.

Although we may see more developments that change the circumstances and opportunities, we feel it is important to inform you now of our position on defining ME/CFS.

Simply, our position is as follows:

- Only ME/CFS experts have the experience and knowledge to define the disease.
- A consensus of experts and the medical professional community at large on how to diagnose the disease is greatly needed.
- The 2003 ME/CFS Clinical Working Case Definition, Diagnostic and Treatment Protocols (also called the "Canadian Consensus Criteria" or "CCC") is far superior to the more commonly used 1994 International Case Definition (Fukuda) or Oxford definition, but the current state of scientific knowledge has shown a clinical definition with biomarkers and treatment subgroups is now possible and needed.
- A definition that tells how to distinguish those with severe functional limitations is needed.
- Any effort to improve the definition must include replacing the "CFS" moniker.
- At least three different definitions are needed: a clinical definition, a more narrow research definition, and a clinical pediatric definition, and these should be developed together from the same initiative.

All the recent flurry of activity stems from the government's action after an October 2012 Chronic Fatigue Syndrome Advisory Committee (CFSAC) unanimous recommendation:

"Promptly convene (by 12/31/12 or as soon as possible thereafter) at least one stakeholders' (Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS)experts, patients, advocates) workshop in consultation with CFSAC members to reach a consensus for a case definition useful

for research, diagnosis and treatment of ME/CFS beginning with the 2003 Canadian Consensus Definition for discussion purposes.”

Why Do We Need to Give Attention to the ME/CFS Definition(s)?

We agree with a September 23, 2013 letter signed by 35 ME/CFS experts: “... in recent years expert researchers and clinicians have increasingly used the CCC, as they have recognized that the CCC is a more scientifically accurate description of the disease.” The 2003 CCC is better than the Fukuda and Oxford definitions because it identifies patients with this neuro-endocrine-immune disease as separate from those with similar symptoms, including fatigue, of an unknown or another disease.

However, despite the International Association of CFS/ME (IACFS/ME) years ago endorsing the 2003 CCC and it being used in research, we note the following:

- Main street clinicians of all specialties do not use the 2003 CCC or even know about it.
- None of the medical professional organizations representing a medical specialty have embraced the 2003 CCC or distribute information about it to their members.
- It is not taught in medical schools.
- The Centers for Disease Control and Prevention has said they will only endorse an ME/CFS criteria that is “data driven” from a study, which they are now conducting.
- The CCC continues the harmful name for the disease, “chronic fatigue syndrome.”

These obstacles are what prompted the unanimous CFSAC recommendation and a subsequent government contract with the Institutes of Medicine (IOM) to create a consensus on a clinical definition.

This situation and lack of consensus is not unusual. According to Rear Admiral Sandra L. Kweder, with the Food and Drug Administration, other diseases that faced the same or similar challenges include irritable bowel syndrome, functional dyspepsia, depression, prostate cancer and fibromyalgia. Research progress is being made in these diseases because “a generally agreed-upon definition with signs and symptoms and measurement tools could be employed for that condition were agreed upon, developed and then there was able to be movement forward,” she said at the October 2012 CFSAC meeting.

What’s the difference? Except for fibromyalgia, all of these other conditions fall under an existing medical specialty that includes professional certification. So a medical professional organization for that specialty can endorse a science-based definition, and it will be accepted by members of that specialty, the ones who provide medical care for patients with those diseases. Although the American College of Rheumatology has stated clinical care for fibromyalgia patients falls under primary care providers, this organization of an existing medical specialty that includes professional certification has endorsed a definition created by rheumatologists that did a study.

Because ME/CFS is a dysfunction in more than one body system, no medical specialty with certification has embraced the disease, nor a medical specialty organization.

After urging the adoption of the 2003 CCC, the recent letter signed by 35 ME/CFS experts also says, “The expert biomedical community will continue to refine and update the case definition as scientific knowledge advances; for example, this may include consideration of the 2011 ME International Consensus Criteria...”

We believe science has progressed so that the 2003 CCC needs to be updated now. Yet the letter does not state what these professionals plan next or what mechanism is in place to create a consensus of an up-to-date definition, get the endorsement of other medical professional organizations and the CDC and get all clinicians to embrace it and develop a better name for the disease. Papers published in medical journals just continue the debate instead of bringing consensus of experts and the medical community at large. More action and leadership is needed to bring this about.

Who Should Take the Lead in Creating a Consensus on an Up-to-date Definition?

In response to the CFSAC October 2013 recommendation, the U.S. Dept. of Health and Human Services Office on Women’s Health announced their contract with the Institutes of Medicine (IOM) that, at first, had very little information. The second announcement includes many of the goals we listed above. However, we have concerns because the U.S. government has a history of misguided research, lack of commitment, mishandling research funds and ignorance of our disease because of not collaborating with patients or with outside ME/CFS clinical and research experts.

The September 23 announcement of the IOM contract says those on the committee “will include approximately 15 members with expertise in the following areas: epidemiology; clinical medicine/primary care and other health care fields, particularly with expertise in ME/CFS, including neurology, rheumatology, immunology, pain, infectious disease, behavioral health, cardiology, endocrinology; and scientists and physicians with experience in developing clinical case definitions.”

Yet we still have a concern because the announcement does not list which experts or how they would define someone with expertise in ME/CFS. Because there is no certification or specific education for an ME/CFS expert, we define an ME/CFS clinical expert as a doctor who has **primarily** provided clinical care to ME/CFS patients for at least 10 years. We define an ME/CFS research expert as someone who **primarily** researches ME/CFS, particularly ME/CFS researchers who have published on biomarkers and definitions.

We are pleased to see the experts the Centers for Disease Control and Prevention (CDC) are using in their Multi-site Clinical Assessment of CFS, including our organization’s medical advisor, Dr. Andy Kogelnik. This came after our organization sent a 2011 letter to Dr. Elizabeth Unger at the CDC urging her to start working with clinicians who have primarily cared for ME/CFS patients for years. Also, the 2011 National Institutes of Health ME/CFS State of the Knowledge Workshop mostly had true ME/CFS

experts as we would define them. The Food and Drug Administration included some experts as we would define them in their April 2013 ME/CFS Drug Development Scientific Workshop.

Meanwhile, we have noticed some of the most recent appointments to the CFSAC are not individuals who primarily research or provide clinical care for ME/CFS patients. We are even concerned that some of them do not realize that post-exertional increase in symptoms is a cardinal symptom of the disease. While these should be experts advising the secretary, some have had to be educated on either the history of ME/CFS in the government or of the disease itself.

Additionally, many Gulf War illness advocates were very disappointed that the IOM failed to include neurological, endocrine and immune system Gulf War illness experts on the panel designed to create a case definition for that disease. This increases our concern.

As far as the IOM contract for ME/CFS, the stakes are too high, trust has not been earned, and patient advocates were not involved in the formation of this contract.

We think Dr. Nancy Lee, the CFSAC designated federal officer, said it best: “Nothing about me without me.” Clearly, the people who are most impacted by a disease definition are the patients. Clearly, the people who are most impacted by a bad definition are the patients. Patients or patient organization representative should be included in all government negotiations for contracts on initiatives that pertain to this disease. Such a step would increase patient trust in government actions.

We have the highest respect for the International Association of CFS/ME (IACFS/ME) as an organization of medical professionals with expertise in ME/CFS. Even though it does not include a certification that reflects specialty training and thus does not hold the same influence that other professional organizations for medical specialties hold, it has advanced knowledge of ME/CFS through the bi-annual scientific conferences and publication of the CFS/ME Primer for Clinical Practitioners. They and the professional members of IACFS/ME are our experts.

Our organization is ready and eager to help the IACFS/ME establish a certification process so other medical professionals have more respect for the IACFS/ME and ME/CFS experts. Our organization is also ready and eager to help the IACFS/ME hold a workshop that leads to a widely accepted, up-to-date, and biomarker-based clinical definition that has subgroups and way to identify those with severe function limitations and a new name for the disease.

Our organization is ready and eager to help the 35 medical professional experts who signed the letter mentioned above to hold a workshop that leads to a widely accepted up-to-date biomarker-based clinical definition that has subgroups and way to identify those with severe function limitations and a new name for the disease.

One suggestion is for ME/CFS experts or the IACFS/ME to partner with an association of a medical specialty in developing such a workshop. Whatever group of ME/CFS experts takes the lead in accomplishing this, it must include a plan for engaging and getting the support of other medical

professional organizations, the CDC and medical school deans in order for it to have the widest positive impact on patients, most of whom are not under ME/CFS expert care.

What Should Be the Goals of Any Definition Initiative?

Include developing a consensus on an up-to-date research, clinical and pediatric definition in the same workshop – Numerous researchers tell us that a research definition should be narrower than the clinical definition. A narrower research definition ensures a more pure cohort, which will more likely lead to more biomarker discoveries. However, it would be a mistake to have one group of experts develop a research definition and another group develop a clinical definition for such a heterogeneous disease with abnormalities in different body systems and varying symptoms. A research definition should just be a narrower version of the clinical definition. Also, pediatricians who specialize in ME/CFS have published proposed pediatric definitions that differ from the adult definitions. But a consensus is also needed on a pediatric definition.

Distinguishing between ME/CFS and others with symptoms of unknown or of another disease – We now know that the Fukuda, Oxford and some other purported definitions fail to clearly distinguish between people with ME/CFS and those with chronic fatigue of unknown cause or other fatiguing conditions, particularly depression, deconditioning or functional disorders.

It is a mistake to think of ME/CFS as part of a spectrum disorder primarily identified with fatigue. As the CDC states on its continuing medical education course on their website, “Diagnosis and Management of Chronic Fatigue Syndrome,” some ME/CFS patients may come to a clinician with a primary complaint of pain. At the Food and Drug Administration ME/CFS Patient Focused Drug Development Meeting in April, many patients reported that cognitive dysfunctions are often the main illness feature preventing them from being able to function. “The symptom I chose that is most significant in me in my daily life is confusion,” said Joseph Landson, a patient on the panel.

Additionally, many ME/CFS patients do not have constant fatigue. This is why ME/CFS experts describe the “push and crash” experience as a feature of the disease.

ME/CFS expert and Johns Hopkins professor of pediatrics, Dr. Peter Rowe, described the periods of energy a patient may experience in his 2013 presentation to the Chiari and Syringomyelia Foundation: “People will see somebody muscling through an inning or two of the family softball game on July 4 but not understand why that person is in bed for two days.”

Thus, patients with chronic fatigue from burnout, depression, deconditioning or another disease or unknown disease should be clearly separated out from ME/CFS patients because their experience is different and the treatments will be different, particularly in the area of exercise. Studies show a deconditioned person with fatigue improves his aerobic performance with exertion, but an ME/CFS patient loses aerobic function after exertion. Failing to distinguish these patients based on their different conditions is a disservice and harmful to all these patients.

Subgrouping for treatments – Many ME/CFS possible subgroups have been identified by researchers that could guide clinicians to appropriate treatments. These include active infections or lack of active infections, blood pressure fluctuations or not, immune system abnormalities and hormone abnormalities, among others. Recent research shows how long a person has had the disease determines differences in immune system abnormalities.

Many diseases are subgrouped, such as hepatitis, breast cancer and diabetes. These subgroups help to identify what treatment should be given to those patients.

Dr. Francis Collins, National Institutes of Health director, said at the 2011 NIH ME/CFS State of the Knowledge Workshop: “There’s no question that this disorder needs further definition, because my sense is there are probably many different potential causes all lumped together into a definition that is probably broader than pathobiology would want it to be. But we need to understand a lot more about what subsets might exist in this circumstance in order to have a better sense of how to intervene.”

Include biomarkers – The symptoms found in many of the definitions are also found in other diseases, particularly fatigue. A 1996 study, titled “Chronic fatigue complaints in primary care: incidence and diagnostic patterns,” says:

“The complaint of chronic fatigue is ubiquitous in the primary care setting. Because of the nonspecific nature of chronic fatigue, practitioners do not focus on this complaint.... From these data, the investigators conclude that the workup for chronic fatigue is often incomplete or lacks documentation.... Also complicating the evaluation process are the multiple associated disorders, the prevalence of the complaint, and the cost/benefit issues facing the primary care physician.”

Because the symptoms ME/CFS patients experience are also seen in other diseases, clinicians need an easier method for distinguishing ME/CFS patients from these other patients, particularly those with primary depression. The misguided focus on fatigue has contributed to less than 20% of ME/CFS patients being diagnosed, which means they are either not receiving treatment or receiving inappropriate and possibly harmful treatments. A biomarker, biomarkers or biomarkers in combination with symptoms will greatly reduce this problem and distinguish it from other disorders.

An emphasis should be on the biomarkers associated with the disease cardinal symptom of post-exertional malaise (in increase of all symptoms resulting from mental or physical activity).

Identify those with severe functional limitations – The level of severity in ME/CFS can vary greatly. Severe cases are mostly bedridden. Yet the 2003 CCC and other ME/CFS definitions do not have a severity scale. Other diseases, such as multiple sclerosis, have a subgroup for those with severe function limitations.

Despite how disabled some ME/CFS patients are, they are not included in the Social Security Administration’s list of Compassionate Allowances. Yet malignant multiple sclerosis is included in that

list. The impact on ME/CFS patients of being denied disability when they are severely limited impacts their family, their living conditions, their access to healthcare, and more.

Rename the disease – Any initiative to create a consensus on ME/CFS research, clinical and pediatric definitions will set a precedent. If done right, it will be a “game-changer.” With the illness primarily characterized with biomarkers, we can dispense with the harmful, belittling and confusing label of “chronic fatigue syndrome.” This is one area where we already have a consensus. The name must go for the following reasons:

- It does not convey the severe impact of the symptoms on the patient’s function and life.
- It implies someone who just gets tired a lot, not an accurate understanding of the disease.
- It focuses on just one of the disease symptoms, which is unique in the names of all diseases.
- It confuses the public and even clinicians and researchers into thinking that chronic fatigue of unknown cause or chronic fatigue of other diseases is the same as chronic fatigue syndrome, making them think that chronic fatigue syndrome is not a distinct illness.

The best analogy is if pneumonia was labeled “chronic cough syndrome” or diabetes was labeled “pee too much syndrome.” Such labels would minimize very serious illnesses. When patients say they have chronic fatigue syndrome, we often hear back from someone who is working too much, “I think I have that,” or “Doesn’t everyone have that?”

We also reject efforts to combine Gulf War illness and ME/CFS under a label of “chronic multi-symptom illness.” Many illnesses are chronic and have multiple symptoms. This label does not add clarity. However, both diseases could appropriately come under an umbrella term of “neuro-endocrine-immune diseases” because they are a simultaneous dysfunction of these systems and the control center for these systems. The attitudes of the labels were published in a 2003 study: “Chronic fatigue syndrome versus neuroendocrineimmune dysfunction syndrome: differential attributions.” The federally appointed Name Change Workgroup developed the umbrella term “chronic neuroendocrineimmune dysfunction syndrome” and suggested subtypes.

The harm that “chronic fatigue syndrome” label has done to public and clinician understanding of the disease, research funding, and stigma on patients cannot be overstated.

We welcome any comments or questions on this position statement. Contact us at info@pandoraorg.net.