

The panel has requested that the public submit their comments on the P2P Draft Report, I am respectfully submitting the following comments and corrections on the Report. Please note that I am using the line numbers from the P2P Draft document found at: <https://prevention.nih.gov/docs/programs/mecfs/ODP-MECFS-DraftReport.pdf>

Correction: Line 50 - “163 symptoms have been associated with ME/CFS.” This is an **incorrect** paraphrase of Dr. Luis Nacul’s presentation on December 9th, in which he stated that using the Fukuda (1994 CDC definition), there were 163 *permutations* of symptoms. *What Dr. Nacul meant was that there were 163 possible combinations of symptoms using the Fukuda criteria that could be used to diagnose ME/CFS.* Dr. Nacul, and others, have pointed out that *because there are so many possible permutations, and because PEM is not required to be present, the Fukuda criteria may capture people who do not have ME/CFS, but may have other fatiguing illnesses*, including early MS and undiagnosed cancer. (Dr. Nacul also pointed out in his presentation that **when PEM is required the number of permutations in the Fukuda definition drops to 35.**) Dr. Smith also observed in her presentations that the Fukuda criteria capture less impaired people, possibly those with deconditioning and depression.

Amend: The Report should recommend that the Fukuda definition be retired, along with the Oxford definition, and replaced with the Canadian Consensus Criteria for ME, which is the definition used by the world’s leading ME/CFS clinicians and researchers.

Correction: Line 113 – “Existing treatment studies (cognitive behavioral therapy [CBT] and graded exercise therapy [GET] demonstrate measurable improvement” and Line 348 -9 “The modest health benefit of CBT should be studied...” No studies demonstrating benefits from CBT or GET were included in the AHRQ review. As Dr. Smith pointed out in her presentation on December 10th, **none of the studies on GET or CBT used patients fitting the criteria for ME.** In addition, the forest plot shown in Dr. Smith’s presentation on December 10th indicates **that the only studies to demonstrate benefits from CBT were Oxford-based studies, which were *then* averaged with the studies which showed little if any benefit in order to yield an overall positive result.** In systematic reviews, averages are rarely used for such small numbers of studies, because, as is demonstrated by Dr. Smith’s forest plot, averages produce unreliable results -

Amend: The Report should amend this statement to specify that improvements were only found in patients diagnosed using the Oxford case definition for CFS in the UK. The report should also acknowledge in these two lines that the panel has recommended that the Oxford case definition be retired because it captures people who do not have ME or CFS.

Correction: Line 92 – “Although psychological repercussions (e.g. depression) often follow ME/CFS ...” Dr. Natelson’s presentation on subtyping showed distinct objective markers between ME/CFS, major depressive disorder (MDD), and fibromyalgia (FM) indicating that there are NOT substantial overlaps with either condition. Dr. Klimas’s presentation on subtyping showed that in a group of 960 ME/CFS patients the most common comorbidity was FM, not depression. Her research shows that depression does not often follow ME/CFS. Psychometric testing shows that patients with ME/CFS score much better on role emotional than patients with depression. Dr. Jason has also observed a striking difference in patients with depression and patients with ME/CFS, which is that when asked what they would do if the illness were to disappear, patients with depression say “I don’t know,” whereas patients with ME/CFS will provide a list. There is, to date, no valid psychometric instrument that has shown that depression, MDD, or any other psychiatric conditions frequently occur either with or after ME/CFS.

Amend: The Report should delete the statement that depression often follows ME/CFS.

Correction: Line 95 “Focusing on fatigue alone may identify many ME/CFS cases.”

This statement is incorrect. Focusing on fatigue alone may identify many chronic fatigue patients, including people with leukemia, MS (1/3 of patients with early MS present with fatigue as a primary symptom and are misdiagnosed with CFS), incipient cancers, Hashimoto’s disease, Ehlers-Danlos, and a multitude of other illnesses. Focusing on fatigue alone not only has led to the misdiagnosis of significant numbers of patients with other treatable conditions, it does **not** identify many ME/CFS cases. The symptom that identifies ME/CFS patients is post-exertional malaise, also known as post-exertional collapse or Neuro-immune Exhaustion. As Dr. Jason and Dr. Nacul pointed out, this is the hallmark symptom of ME/CFS.

Amend: The report should revise this statement to “Focusing on PEM may identify many ME/CFS cases.”

Correction: Line 32 “ME/CFS exists.” This statement is only partially correct.

Myalgic encephalomyelitis is a neurological disease that was described by Dr. Melvin Ramsay in the 1950s. It has occurred in many outbreaks and clusters since the 1950s. ME has two case definitions, both of which require PEM, and both of which accurately describe the patient population. Chronic Fatigue Syndrome does not exist as a medical entity. There is no case definition for CFS that describes a group of patients distinct from any other group of patients with fatigue.

Amend: The Report should delete the sentence “ME/CFS exists.” The Report should recommend that the term “CFS” be dropped,

as it does not describe a distinct clinical entity, and it should be replaced by Myalgic Encephalomyelitis, with its corresponding case definition (the CCC).

Additional notes

Since 1969, Myalgic Encephalomyelitis has been listed in [Diseases of the Nervous System](#) of the [WHO ICD](#) (World Health Organization International Classification of Diseases), current diagnostic code, [G93.3](#) (323.9 in the US).

Many tests can show the effects of ME Including: A **two day CPET**, [SPECT and PET Scans](#), [Natural Killer Cell Function test](#), [Rnase-Lenzyme dysregulation](#), [Spinal fluid protein abnormalities](#), [Blood Flow](#). The hallmark symptom is [Post-Exertional Neuroimmune Exhaustion](#) (PENE, in lay terms: post-exertional major exacerbation of symptoms) - exertion being anything from talking or listening, to walking across a room to going to the grocery store, depending on an individual's disease length and severity. Hypersensitivity to even minor sensory stimulation, an almost universal ME symptom, can cause PENE. Orthostatic intolerance (symptoms worsen in an upright position) is also common. These and [many more symptoms](#) usually result in the patient being bedbound or homebound.

<http://www.name-us.org/ResearchPages/ResearchArticlesAbstracts/CirculatoryArticles/2014KellerVO2Peak.pdf>

Betsy A Keller, John Luke Pryor and Ludovic Giloteaux. "The results of this study confirm previous work [13,17,18] that demonstrated an abnormal response to exercise in fatigued ME/CFS patients. The use of a **two-day CPET protocol** to measure the post-exertional response to exercise in ME/CFS allows us to better study the nature of this unusual, debilitating type of symptom exacerbation that follows exertion or stress, often described as post-exertional malaise or neuro-immune fatigue. Additionally, this test protocol yields information that can provide specific guidelines for exertion in ME/CFS patients in order to avoid symptom flares and that may improve daily physical function. ME/CFS patients exhibited significant post-exertional declines in VO₂, work, minute ventilation and O₂ pulse at both maximal and ventilatory threshold intensities. Consequently, classification of functional impairment based on VO₂ peak and VO₂ at ventilatory threshold over-estimated the functional ability of 50% of ME/CFS in this sample when based on only one CPET."

Thank you so very much for considering my comments and corrections. I hope that the final version of the Draft Report will help researchers obtain badly needed NIH funding for continuing and expanding research into the causes, mechanisms, and treatments for patients with M.E/CFS.

Sincerely,

Catherine Berger

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- See more at: <http://cfstreatment.blogspot.com/2015/01/the-p2p-draft-report-pros-and-cons-and.html#sthash.Kp7LWuti.dpuf>

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