

P2P Comment Anonymous #4

Line 2-3, Line 179 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is “a chronic, complex, systemic disease” [Montoya 2014]

Line 3 “characterized by extreme fatigue...” – It is difficult for a symptom common to many diseases to characterize a particular condition or a given disease spectrum. It would be more accurate to say that ME/CFS is “characterized by post-exertional collapse, muscle weakness/fatiguability, cognitive difficulties, and unrefreshing sleep, although other symptoms will be present”. The original wording risks continuing to confuse ICF (idiopathic chronic fatigue) from any undiagnosed (missed diagnosis or currently undiagnosable) cause with ME/CFS. As the current state is, probably ½ of the people carrying a diagnosis of CFS probably have other diagnosable diseases (and in many cases, would have something with a mature treatment protocol with FDA-approved treatments and would be better off under their other diagnosis) [ME Research UK, nd]. “Not improved by rest” is confusing because although it was intended to rule out a condition that could be cured by going on sabbatical [Reeves 2003], it sounds like rest doesn’t provide any benefit, whereas in reality, rest does provide a benefit.

The most important thing this Panel can do for this disease is to characterize it accurately and recommend funding commensurate with the burden of disease (a new QALY study is urgently needed, possibly by the multicenter sites, but it is imperative that severe and other homebound patients are included for accuracy) and specifically targeted to pathophysiology and physiological treatments.

4 The etiology and pathogenesis remain unknown; there are no laboratory diagnostic tests; 5 and there are no known cures.

Replace with: “The etiology and pathogenesis are uncertain, but researchers agree that the immune system is disrupted, and there are no FDA-approved medications designated for the diagnosis, and no treatments shown to have substantial clinical benefit to a large proportion of patients in large studies, although symptomatic treatment is available.” [Medscape Rheumatology, 2015].

(Tests have been covered by the CFSAC submission: I will defer to the researchers on the voting membership about tests.)

[line 6] 1 million people... unmet public health need... [line 7] major disability for a large

proportion affected" [lines 7-9] "Limited knowledge and research funding creates an additional burden" – good job; thank you.

It would be good to clarify that the 1 million people is a US figure only, while ME/CFS is a global problem. I understand that this is a US report, but it's important that the scope of the problem be acknowledged. While researchers in other developed countries such as Australia, Japan, Scotland, and UK do carry out some research into ME/CFS, developing countries such as Nigeria also have a population with ME/CFS and unmet needs, and the global need may influence US spending levels.

Line 6-7 "economic burden estimated to be greater than \$1 billion"

This figure seems to be inaccurate [a proper rounding of the lowest available figure would render \$2 billion, but there are other applicable figures and this one is inadequate by itself]; the CFSAC submission has addressed this well. It's important not to understate the burden because this should influence funding.

line 114 - "measurable improvement" from CBT/GET

This does not seem to be an important measurement. "Improvement" on the big trial mentioned was chiefly answers on questionable surveys (The SF-36 physical function was graded oddly, and both that and the Chalder fatigue scale are known to have floor/ceiling effects; neither is known to be valid for tracking improvement in fatigue), the low curve and pattern of which mimics placebo/ reverse placebo/ experimental error/ regression to the mean/ bias. Also, it was more difficult in the PACE trial to register a deterioration than an improvement [Kindlon 2012]. Given the positive tone of the authors compared to the very weak data, this trial (and all the papers it generated) could be an example of Researcher Allegiance [Ben 2013].

The other "improvement" was on 6-minute walk test, on which CBT got no better result than usual care. In GET, even with the minimal improvement during the trial, patient performance was similar to that of people with serious illnesses like congestive heart failure and COPD. (See graph at <http://evaluatingpace.phoenixrising.me/sixminwalk.html>); some more ways the graphs and

other data from the trial were tricky is shown in graph form at <http://evaluatingpace.phoenixrising.me/aps3detailsstill.html#a>)

There were no improvements in employment and no reduction in need for health care, custodial care, disability insurance benefits, and so on. Other CBT/GET trials are similar, without being able to demonstrate any tangible benefit.

As you noted in the draft, “this has not translated to improvements in quality of life (QOL),” and this is probably because the improvements as measured are artifactual.

This is not to say CBT or supportive counseling has no place: but it must be noted that there are various kinds of CBT. CBT which attempts to convince a patient she is not actually ill with anything more serious than misperceptions and sequelae of deconditioning (much of the CFS literature on the topic, although there are some exceptions) is inappropriate and should be excluded from treatment recommendations for poor ethics (not to mention poor methods). CBT or supportive counseling which helps one cope with the actual reality one faces should be available, but should not be billed as a treatment “for” the disease or listed in an official protocol for the disease, as it is no different from the case with multiple sclerosis, Lupus, narcolepsy, or heart disease (and I do not typically see counseling or CBT listed in treatment strategies for these), that patients have a difficult life and some may wish to talk with a professional counselor.

Educational efforts are needed to help patients and their health care providers better understand 79

this disease and scientific processes. The scientific community also has a responsibility to 80

address issues that are meaningful to patients.

Educational efforts are great for doctors, allied health professionals, social services, the general public, etc. Thank you. They do need to be based in the physiological research. Patients already know a lot, usually more than anyone else on their healthcare team, and there is probably little that patient education can do at this time.

Thank you for mentioning the responsibility of the scientific community. DHHS also bears this responsibility, and to some extent so do individual doctors.

Studies investigating 273

homeopathy, non-pharmacologic, complementary, and alternative medicine 274

treatments are needed. Studies addressing biopsychosocial parameters (including the 275 mind-body connection), function, and QOL should be encouraged.

The modest benefit 348

from CBT should be studied as adjunct to other modalities of treatment such as self-349 management. Future treatment studies should evaluate multimodal therapies.

Psychopathology, CBT, mind-body research, self-management, and the like has already had its day and failed to produce any meaningful results (except that pacing does make us less miserable and in most of us, doesn't provoke the disease as much as pushing, but activity management is not a treatment by any means). These recommendations should all be struck and replaced with an emphasis on physiopathology, biomarkers, and pharmacology. Studied treatments should be mostly pharmaceutical, but could also include some CAM such as vitamins, antioxidants, herbs, and myotherapy.

We believe ME/CFS is a distinct disease 303

that requires a multidisciplinary care team (e.g., physicians, nurses, case managers, social 304

workers, psychologists) to optimize care.

This list seems unrepresentative. I have an internal medicine doc as my primary care doctor, as well as a nuclear cardiologist (the regular cardiologist couldn't figure out how to help me), a pulmonologist, a rheumatologist, a gastroenterologist, a myotherapist, and sometimes an integrative medicine specialist. I should have a neurologist but I can't find one who is comfortable with my CFS diagnosis, except the first one who diagnosed me but I cannot see him now because of insurance peculiarities. An immunologist might be a better choice than a rheumatologist, I don't know, but would like to have that option. Although most of the professionals I mentioned are "physicians", a "multidisciplinary care team" sometimes includes different kinds of physicians, as well as the types of professionals mentioned. We need to recruit more kinds of specialists to have an interest in ME/CFS, and we need a specialist home for it. Also need an NIH Institute home.

References:

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Reeves WC, Lloyd A, Unger ER, et al. and the International Chronic Fatigue Syndrome Study Group. Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution. *BMC Health Services Research* 2003, 3:25

Montoya J. (2014) Stanford Unravels the Mysteries of Chronic Fatigue Syndrome. <https://www.youtube.com/watch?v=pvtbsStLQWk>

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NB: there is a CDC study showing a similar phenomenon in the US, but I do not have the study to hand.