

COMMENTS ON: DRAFT EXECUTIVE SUMMARY
NATIONAL INSTITUTES OF HEALTH

Pathways to Prevention Workshop: Advancing the Research on Myalgic
Encephalomyelitis/ Chronic Fatigue Syndrome

December 9–10, 2014

Susanna Agardy*

The draft summary reflects contradictory views on the nature of ME/CFS. On the one hand, it recognises the seriousness of ME/CFS (lines 82-86), the importance of post-exertional malaise (PEM) and neurocognitive deficits (106-7) and the overemphasis on fatigue (95-7). The recommendation to retire of the Oxford Criteria (OC) (364-66) and the focus on patient-centred efforts (eg. 166-67, 184, 187-191, 134-46) are welcome. On the other hand, it proposes the inappropriate treatments CBT/GET used in the biopsychosocial prescription (eg, lines 115-16).

I offer my comments on these contradictions and other issues of concern.

1.a.) The observation is made that CBT and GET ‘...demonstrate measurable improvements, but this has not translated to improvements in quality of life (QOL).’ (113-16) In view of the admitted failure of these treatments to translate it is difficult to understand why they should be used at all for ME/CFS.

Harms have been recognised in the Draft Review¹. Kindlon² and Twisk et al³ provide extensive summaries of the risks and harms of CBT/GET. If CBT/GET are found to be ineffective or harmful they will remain so regardless of the name of the treatment strategy of which they form a part- primary treatment or multimodal therapy. Post-exertional malaise (PEM), recognised in this draft report (106-7), prohibits GET^{2,3}. Perhaps it could be used for rehabilitation when there is recovery from the underlying disease.

b.) The use of the term ‘QOL’ understates the PACE finding that following 52 weeks of GET treatment patients could cover a shorter distance in the 6 Minute Walking Test (6MWT) than patients with heart failure and those awaiting lung transplant^{4,5}.

c.) CBT/GET treatments are designed for OC-defined fatigue conditions and ‘assume that the syndrome is perpetuated by reversible physiological changes of deconditioning and avoidance of activity’ with ‘increased perception of effort, leading to further inactivity. Fear of exercise is assumed to be the driver of this supposed condition⁴. These descriptors do not apply to ME and it would be illogical and unethical to apply these treatments to ME^{3,6,7}. The recommendation perpetuates the legacy of the OC even while its retirement is recommended (364-66).

d.) The ‘patient-centred QOL outcomes’ (331-32) and the definition of end-points (157-58) which are called for need to include objective measures of treatment outcomes eg, measures of walking ability, actometer-based measures, work ability, etc. Quality of life for patients means the basic ability of being able to be active without the repercussions of PEM. Patients’ priorities should be attended to (277-78). As patients well know, feeling

better, which might register on tick-a- box tests, does not mean being able to do more. This is observed by the authors of PACE: `objective measures of physical activity have been found previously to correlate poorly with self-reported out-comes.’⁸

It is notable that there appears to be no self-report scale of physical ability tailored specifically to ME. At least the SF-36 physical function scale could be adapted to accommodate PEM by asking how many of the activities a patient can do in one day and without repercussions.

2. In keeping with the recommendations to keep patients involved in a meaningful and ethical way (184-85, 188) the risks of any treatment in a clinical or experimental setting must be explained to patients. The CBT/GET studies are notably lacking in this regard. For example, in the PACE Protocol patients are told that the treatments are safe and beneficial. Kindlon explains, quoting Cooper et al, “like pharmaceutical therapies, prescribing exercise as therapy, an activity that is gaining in acceptance throughout the medical community, must be predicated on understanding the risks and benefits of exercise as thoroughly as possible.”² This risk is a central concern in ME where the distinguishing feature is PEM.

3. a.) The draft summary recommends that ‘the modest benefit from CBT should be studied as an adjunct to other modalities of treatment such as self-management’ (348-50). It is unclear what kind of CBT the authors have in mind. CBT may be beneficial insofar as it is aimed at assisting patients to adjust to their chronic state of illness, combined with supportive approaches. This should be distinguished from the type of CBT practised in the OC-defined studies which aim to remove fear of exercise and to dissuade patients from their beliefs that their illness has a biomedical basis⁴. This type of CBT then encourages them to practise GET, exposing them to risk. If patients have learned to fear certain levels of activity for good reason this approach is disrespectful of their learning from experience and responsibility for self as well as invalidating the patient.

b.)The aim of CBT treatment needs to be considered. The PACE trial results show that the cognitive behaviour therapy group performed even worse than the GET group in the 6MWT and showed no improvement compared with the specialist medical care only group^{4,5}.

c.)There may also be difficulties in administering CBT to patients with concentration and memory problems. There appear to be no studies which examine brain-fogged patients’ ability to withstand a session requiring focus and challenges to their thinking. The level of stress this may induce should be considered. The OC do not include cognitive dysfunction symptoms¹⁰ and its customary treatments should not be transposed to ME without careful examination of costs and benefits to the patient.

4. a.) It is unclear what contribution ‘Studies addressing biopsychosocial parameters (including the mind-body connection)’ (275-76) are expected to make. The biopsychosocial perspective encourages the diagnosis of psychosomatic disease, particularly in the absence of a clear diagnostic test. For ME/CFS it has been refuted by

Twisk et al³. Once the tests administered to a patient presenting with ME/CFS symptoms show that ‘all tests are normal’ the default diagnosis of psychosomatic illness is frequently provided. Or, as Hyde points out, patients may first be given the CFS diagnosis: since CFS is diagnosed after the exclusion of other medical conditions the psychosomatic diagnosis remains, by default¹¹. Either way, the patient is stigmatised and condemned to a future of having their missed diagnoses and misdiagnoses perpetuated¹¹.

b.) Some tragic experiences in the history of ME/CFS have resulted from the biopsychosocial approach. The video ‘Voices from the Shadows’ tells the stories of several severely affected patients whose lives have been greatly worsened by the psychiatric approach and the disbelief accorded to those with ME or CFS¹².

c.) Thus far, as applied to ME/CFS, this model has consisted mainly of the attribution of motives to patients, evidence-free (see 1.c.). On the basis of these attributions patients have been subjected to the crude form of behaviouristic intervention where CBT/GET have become the stimulus to which they are supposed to produce the response of becoming economically productive units (we wish). The underlying medical conditions have been ignored. This approach has not been effective and has deprived patients of dignity and validation.

d.)The relevance of the biopsychosocial perspective should be seen in the context of the statement by Thomas Insel, director of the NIMH, who said about the effectiveness of psychiatry: “‘Whatever we’ve been doing for decades, it ain’t working. And when I look at the numbers- the number of suicides, number of disabilities, mortality data – it’s abysmal, and it’s not getting any better. All of the ways in which we’ve approached these illnesses, and with a lot people working very hard, the outcomes we’ve got to point to are pretty bleak- especially’, he added, ‘compared with the “extraordinary” progress in other fields such as the 70% drop in mortality from cardiovascular disease’ since he went to medical school ‘or the steep reduction in deaths from auto accident and homicides...’ ” and we don’t know which treatments are working for which people.”¹³ (pp 350-51) dimensions of observable behavior and neurobiological measures’ as well as other biomedical techniques in the search in <http://www.nimh.nih.gov/research-priorities/rdoc/nimh-research-domain-criteria-rdoc.shtml>

e.) The biopsychosocial perspective has already had immense influence on the research on ME/CFS, using up funds without tangible benefits. In view of the urgency for research in the biomedical sphere this perspective should not be given priority. The vote of no confidence in conventional psychiatric diagnosis by the NIMH should further deter any intentions to take a biopsychosocial route in the search for insight into ME/CFS.

5. The draft summary states that ‘...this is not a psychological disease in etiology.’ (92-93) The proponents of the OC also agree with this. The controversy lies in the beliefs about the causes of the perpetuation of the disease. The OC proponents claim that patient themselves perpetuate the condition causing their deconditioning (See 1.c.). These assumptions persist even in the face of their own studies’ failure to confirm the assumed

underlying features, especially deconditioning. It is unsettling to note the ambiguity left hanging in the above statement (92-93). This incomplete statement allows an interpretation which leaves in doubt the acceptance of serious physical disturbances in ME/CFS noted elsewhere (82-86).

6. The draft report rightly points out the need for the training of physicians and other therapists. Not only do they lack the knowledge for instructing patients in self-management and GET (131-38), anecdotal evidence also suggests that the instructions they issue are often inappropriate and damaging. They frequently push uninformed, desperate patients keen to do anything to get better, far beyond their limits through unhelpful goal-setting strategies, insisting on increased activity, thereby making them worse.

The key issue is PEM: professionals need to believe and understand the symptoms peculiar to PEM, the concept of which is frequently foreign to them. They also need to learn that it is best to work with the patients, respecting their limits and feedback and teaching them to listen to their bodies (as in pacing). The draft summary's emphasis on patient-centred therapy is important for this scenario. For ME it is GET per se which is inherently dangerous and attention should not be shifted to patient attitudes as the cause of problems (135-37).

Self-management (130-31) is necessary. However, in spite of embellishment with euphemisms like 'empowerment' the prescription for it still sends the message, 'we can do nothing for you'. In practice, patients are left to cope as best they can, with perhaps a few guidelines which may or may not be appropriate.

7. The draft summary refers to the desirability of a 'multidisciplinary care team' (303-05). A patient's wish list would ask for multidisciplinary teams composed of ME specialist and well-informed specialists in say, neurology, cardiology, immunology, gastroenterology, etc, as required. Well-qualified and sympathetic specialists, as well as acceptance of ME by the welfare systems of each country may leave less work for other types of multidisciplinary care teams. These teams must also keep the medical condition firmly in focus and avoid unproductive excursions into the psychosocial sphere.

8.a.) As pointed out in the summary, the focus on fatigue (95-97) should be replaced by greater emphasis on PEM and neurocognitive deficits. PEM is the distinctive marker of ME, it is delayed, it can occur in response to very minor exertion, depending on the severity of the disease of the patient. Importantly, PEM is not a unitary symptom but includes the resurgence of numerous symptoms which do not follow exercise in a healthy person, eg, sore throat, headache, tingling, increased brain fog, increased sensitivities to sound, light, foods. The symptoms may be changeable and last for an inordinate time.

b.) Broad research question: how does exercise trigger such a variety of symptoms? Snell et al¹⁴ and others have begun to uncover underlying issues and these findings need to be further pursued.

c.) The dominant and vague term 'fatigue' is confusing and does not describe the symptoms. As the draft summary recommends, patients' language should be attended to (eg, 184-91). Patients speak of 'massive crash' 'feeling terrible', 'flu-like symptoms', 'brain fog', 'having no energy', 'needing to rest', 'dizziness', etc, rather than fatigue. Orthostatic intolerance also produces the desire to lie down and can be interpreted as fatigue. Sometimes patients have difficulty describing their symptoms and they may settle for 'fatigue'. As with PEM, the more specific symptoms should guide the research.

d.) According to Hyde, a diagnosis of fatigue, as in 'CFS is a mistake because it treats fatigue as if it was a disease in itself, which it is not. It indicates only that something is wrong. Patients with fatigue should have a thorough examination beyond basic tests. "...the various definitions of CFS actively impede physicians' ability to make a rapid diagnosis and a scientific confirmation of the illness, thus preventing a possible immediate treatment of some of these significantly disabled M.E. patients." 11

9. Some parts of the draft summary may create the impression that less is known about ME/CFS than is the case (2-5). Unfortunately, much of the existing biomedical research was not acknowledged in the Review Draft Report to AHRQ 1 because these projects did not achieve more than they did while facing obstacles in funding and support. Due to the acceptance criteria for the AHRQ report the OC-based studies emerge as dominant, distorting the evidence-base. The biomedical research needs to be given credit for discovering numerous abnormalities and possible markers and laying the groundwork for sub-group research, as pointed out by Dr Klimas at the Workshop.

10. According to the draft summary, 'The symptoms patients consider clinically meaningful are not in the scientific literature; this discordance must be rectified.' (166-67) The most important symptoms and those reported by patients are already listed in the Canadian Consensus Criteria and its revisions. 6,7. These criteria are based on specialist doctors' encounters with some 50,000 patients. They do indeed, reflect patient experience as is recommended at lines 184-85. These criteria are the only ones which acknowledge these symptoms. Their use in research and diagnosis would go a long way to rectifying the problem identified at 166-67.

11. Once the focus is concentrated on patients' particular symptoms and the limited usefulness of 'fatigue' as a definition of ME/CFS is recognised, the frivolous and misleading name Chronic Fatigue Syndrome can also be retired and the way can be cleared for a more precise definition along the lines of the CCC and ICC 6,7.

*My comments are based on following the research and events in ME/CFS, my own long-standing experience of ME and communication with other patients. I have a background in social research.

References

1. AHRQ Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
Draft Review Report 2014
2. Kindlon T, Reporting of Harms Associated with Graded Exercise Therapy and Cognitive Behavioural Therapy in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
Bulletin of the IACFS/ME. 2011;19(2): 59-111
3. Twisk FN, Maes M, A review on cognitive behavioral therapy (CBT) and graded exercise therapy (GET) in myalgic encephalomyelitis (ME) / chronic fatigue syndrome (CFS): CBT/GET is not only ineffective and not evidence-based, but also potentially harmful for many patients with ME/CFS. *Neuro Endocrinol Lett.* 2009;30(3):284-99.
4. White PD, Goldsmith KA, Johnson AL, Potts L, Walwyn R, DeCesare JC, Baber HL, Burgess M, Clark LV, Cox DL, Bavinton J, Angus BJ, Murphy G, Murphy M, O'Dowd H, Wilks D, McCrone P, Chalder T, Sharpe M; PACE trial management group (2011). Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *Lancet* 377, 823-36.
5. Agardy S (2013). Comments on 'Recovery from chronic fatigue syndrome after treatments given in the PACE trial' [letter] *Psychological Medicine* / Volume 43 / Issue 08 / August 2013, pp 1787-1787, Published online: 19 July 2013
6. Carruthers BM, van de Sande M. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Clinical Case Definition and Guidelines for Medical Practitioners. An Overview of the Canadian Consensus Document. Bruce M Carruthers, Marjorie van de Sande. 2005.
7. Carruthers BM, van de Sande MI, De Meirleir KL, et al. Myalgic encephalomyelitis: International Consensus Criteria. *J Intern Med.* 2011;270(4): 327-38. PMID: 21777306.
8. White PD, Goldsmith K, Johnson AL, Chalder T, Sharpe M; PACE Trial Management Group (2013). Recovery from chronic fatigue syndrome after treatments given in the PACE trial. *Psychological Medicine* Jan 31: 1-9 available on CJO2013.
doi:10.1017/S0033291713000020
9. White PD, Sharpe MC, Chalder T, DeCesare JC, Walwyn R and the PACE trial group (2006) Protocol for the PACE trial: A randomised controlled trial of adaptive pacing, cognitive behaviour therapy, and graded exercise as supplements to standardised specialist medical care versus standardised specialist medical care alone for patients with the chronic fatigue syndrome/myalgic encephalomyelitis or encephalopathy, PACE trial protocol: Final version 5.0, 01.02.2006 ISRCTN54285094
10. Sharpe MC, Archard LC, Banatvala JE et al . A report-chronic fatigue syndrome: guidelines for research. *J R Soc Med.* 1991;84(2): 118-21 PMID: 1999813.

11. Hyde B, Missed Diagnoses, Myalgic Encephalomyelitis and Chronic Fatigue Syndrome Expanded Edition 2011

12. Boulton B, Biggs J Voices from the Shadows

<http://www.meassociation.org.uk/2012/03/voices-from-the-shadows-%E2%80%93-watch-the-film-on-your-computer-from-anywhere-in-the-world/>

13. Greenberg G, The Book of Woe, Scribe, Australia 2013

14. Snell CR, Stevens SR, Davenport TE, Van Ness JM (213) Discriminative Validity of Metabolic and Workload Measurements to Identify Individuals With Chronic Fatigue Syndrome. Physical Therapy 27 June 2013 10.2522/ptj.20110368 Physical Therapy