Thank you for the opportunity to comment on this draft P2P report.

My time and energy is very limited. So 1) I have not been able to follow up every detail of the report, and may well also have missed or misunderstood some points, and 2) I have not provided references, but I know the science of ME/CFS quite well overall, and am confident my comments are soundly based.

Sean
16 Jan 2014

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Before getting onto specifics, I do have one comment about the final recommendations the report may make:

We must have objective standards to assess the validity and value of all models and treatments. Relying solely or primarily on subjective measures is not enough, and indeed can be very misleading and dangerous, and even open to abuse.

If I could only recommend one methodological change to the way ME/CFS is studied and managed, it would be to require that at least 50% of reported primary outcome measures in formal studies must be genuinely objective.

The failure of this field of medical science to meet this minimum scientific standard is what has dragged it into the technical, political, and ethical swamp in which it now wallows, and meeting that minimum standard is the key to getting out of it.

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Detailed comments.

With reference to the 19 page, 403 line version of the draft report:

Lines 1-4, 95-97, and 106-107.
COMMENT: The emphasis on 'fatigue' is problematic. At least four other symptoms need equal consideration as primary defining features of this disease: pain, PEM, and hemodynamic and neurocognitive dysfunction.

Line 4.
COMMENT: There may not yet be a firmly established diagnostic test, but it is becoming clear that two stage testing to account for PEM is likely to be a core research and diagnostic tool.

Line 6.
COMMENT: This figure does not reflect results from several studies of the overall economic burden of ME/CFS, which indicate a minimum figure at least one order of magnitude greater.

Lines 7-51.
COMMENT: Agree.

Lines 52-53 and 88-89.
COMMENT: The reference to the gender imbalance in research is ambiguous and need rephrasing. Presumably it is trying to say that men have not been studied enough.

Line 54, and 89-90.
COMMENT: There is some data on minorities, but possibly not enough to be clear.

Lines 55-73.
COMMENT: Agree.

Line 68.
COMMENT: It is not just pharmacological psycho-therapy that is problematic and often inappropriately prescribed, but also non-pharmacological psycho-therapies as well.

Line 70.
COMMENT: There may be high medication costs, for at least some patients, but there is no good evidence of substantial nor proportional therapeutic benefit, nor broader economic value in those costs.

Lines 72-73. “All of these factors contribute to the poor quality of epidemiologic studies.”
COMMENT: And to poor quality outcomes for patients.

Lines 74-78.
COMMENT: Agree.

Lines 79-80, and 87.
COMMENT: I respectfully suggest the bulk of education needed is for both the professional medical community (clinical and research), and the broader general community. Patients already know their side of the basic story – the fundamental problem is inadequate research, and clinical and community support.

Lines 80—81.
COMMENT: Agree. Patients' views have been basically ignored for far too long, using the unscientific and unethical excuse that we are somehow delusional about our situation, and need to be patronised, infantilised, and re-educated about the 'reality' of it all.

Lines 82-86.
COMMENT: Agree.

Lines 88 and 90-91.
COMMENT: Agree.

Lines 92-106.
COMMENT: Agree. The overwhelming focus on fatigue over the last 3 decades by the medical community, along with the generally grossly underfunded and hence underpowered research, has not been helpful in clarifying the matter. The relationship between ME and CFS and any over lapping conditions needs more attention.

Lines 108-112.
COMMENT: Agree.

Lines 113-117.
COMMENT: All things considered, there is no methodologically robust evidence that CBT and GET offer any primary explanatory or therapeutic power.

At best the data on CBT and GET for ME/CFS proves little more than a small percentage of patients can be persuaded to make small changes in their subjective self-report questionairre-taking behaviour, with no correlating shift in objective measures. It is almost certainly little more than a trivial manipulation of generic psychosocial responses and confounders, and hardly constitutes anything resembling a useful restorative treatment, nor even much of a secondary palliative one.

The value of these two therapies (as used for ME/CFS) have been grossly oversold, and claims about their efficacy and relevance to this disease need urgent and rigorous reappraisal.

Lines 118-131.
COMMENT: Agree.

Lines 131-133.
COMMENT: I don't believe that the average clinician (general or specialist, including ME/CFS specialist,) is currently informed enough to safely offer advice to ME/CFS patients on realistic goals, physical self-awareness, and understanding emotions, and particularly on the role of exercise.

Lines 133-156.
COMMENT: Agree.

Lines 157-159.
COMMENT: Agree. In particular, the distinctions between statistical, clinical, and patient significance need much more robust and detailed exploration, with an emphasis on greater use of objective outcome measures.

Lines 159-161.
COMMENT: The questions must be relevant, unbiased, and unambiguous. This is typically less a matter of patients not understanding, then there being intrinsic problems with the questions themselves, and often with the philosophical framework and theoretical model underlying them. Otherwise I agree.

Also, while patients' views on their condition and situation obviously must be a primary source of data, it is not an infallible source, and patient-reported data must undergo careful objective assessment like any other source of data.

Lines 161-162.
COMMENT: It is not clear to me what the practical meaning or significance is of "prioritizing face-to-face interactions". Also, for many patients this mode of interaction could be quite tiring. Aiming for an appropriately personalised mix of face-to-face and less immediately demanding modes (e.g. email) would be better. The concepts and language we currently have available to describe the experience of ME/CFS, as both subject and observer, are difficult and limited at best, and patients in particular need time to formulate responses.

(This also applies to time frames for patients to properly respond to complex, detailed, and critical documents like this draft P2P report.)

Lines 163-167.
COMMENT: Agree. Especially about the lack of recognition of what constitutes clinically meaningful symptoms to patients. The views of researchers and clinicians about this are not superior to those of patients – the ones who actually have to live with those symptoms.

Lines 168-199.
COMMENT: Agree.

Lines 200-212.
COMMENT: Agree. In particular, I suggest that the placement of ME/CFS in the Office of Research on Women's Health (ORWH) at the NIH is inappropriate and unhelpful to anybody, and needs immediate rectification.

I also emphasise the need for patients to be listened to much more carefully, honestly, and respectfully. The medical profession (clinical and research), and various government authorities, have generally not listened to patients, at a terrible cost to us all. (See also my comments on Lines 131-133 and 157-167.)

Lines 213-221.
COMMENT: Agree, taking into account my comments on complementary and alternative medicine at Lines 281-282 below.

Lines 222-232.
COMMENT: Agree.

Lines 233-241.
COMMENT: Agree. I would also suggest that the search for useful biomedical findings needs to be conceptually broader (though still firmly within mainstream scientific biophysical principles). To find the subtle clues and insights we need to start opening up this problem and cast a wider net of ideas, with input from a range of scientific disciplines (including maybe some extra-medical input, e.g. physicists, chemists, engineers, etc), and of course from patients themselves, many of whom are often better informed of the basic science about their condition than their treating clinicians.

Lines 242-247.
COMMENT: Agree. There needs to be a much better coordinated research effort overall. It is currently far too piecemeal and haphazard, and even feudal at times.

Lines 248-253.
COMMENT: Agree. A comprehensive, robust, independent, and transparent re-analysis of existing studies in this field is needed (including studies dating back to at least the beginning of the 20th century). Clarifying the content and quality of the existing data base will ultimately save time for us all.

Lines 254-280.
COMMENT: Agree.

Lines 281-282.
COMMENT: Disagree strongly. The very limited and precious research money in this field must be spent on studies firmly based in biophysical plausibility. Anything less in the circumstances is scientifically, economically, and ethically irresponsible.

Lines 282-283.
COMMENT: There is no in principle problem with psychosocial aspects being looked at, provided it is done robustly and interpreted fairly, using more objective outcome measures than is typical in these types of studies, and it does not command a disproportionately large amount of research dollars or influence over decisions making.

The existing body of such studies, and the way they are often interpreted, are highly problematic, and a more accurate, less ideological picture of these parameters is urgently needed.

Nonetheless, we now have enough data on this matter to say that any model of ME/CFS invoking primary psychogenesis (as any combination of predisposing, precipitating, or perpetuating factors) is no longer tenable, and we need to more robustly and fully explore different aspects and alternative possible interpretations of any psychosocial features of this disease.

Lines 285-302.
COMMENT: Agree.

Lines 303-310.

COMMENT: Agree. Both research into and clinical management of ME/CFS could benefit enormously from telemedicine. The basic tools are more or less widely available, and for research it is now more a matter of a coordinated data collection project being set up. This is a scalable and hence potentially large scale and long-term project that the NIH could run, probably at relatively low cost.

It is something that could be done as a private-public project, where the NIH fund the coordination and central database, and at least some of the analysis; and patients fund their individual data collection units (given that cost can be held to under about $100-150 USD).

Due consideration must be given to technical standards (including which commercial retail data collection units are best suited), data integrity (including possible deliberate contamination), and patient privacy.

Lines 311-325.
COMMENT: Agree.

Lines 326-327, and 357-358.
COMMENT: The statements to the effect that patients must or should become active in their overall treatment are ambiguous, and could be interpreted in at least two ways: One is that patients are being denied the opportunity to be more active participants and provide more input to the direction of clinical management (and research), and should be much more included in that process. The alternative is that patients have been less than diligent in taking the (alleged) opportunities for treatment, and are somehow obligated to get more involved in the 'team effort'.

The first is acceptable, the second is strongly objectionable.

The meaning these statements needs to be clarified.

Lines 328-339.
COMMENT: Agree. There must be a major change in funding allocation towards a more biophysical based approach, and a very substantial and immediate increase in the quanta of funding for this disease, which is and has always been grotesquely underfunded in comparison to virtually any major medical disorder you care to name, (and a few minors ones too, even one or two that are not really medical problems at all, like male pattern baldness).

The hard data speaks for itself:

http://report.nih.gov/categorical_spending.aspx

Lines 328-349;
COMMENT: Agree. With this additional comment on Line 344 that patient centred QOL outcomes must not be used independent of, or in preference to, more objective measures.

Lines 350-356.
COMMENT: Agree.

Lines 362-363. (See also comments on Lines 248-253.)
COMMENT: Careful reanalysis of the existing literature is needed, and possibly some subsequent and much more methodologically rigorous follow-up studies, before claims of genuinely meaningful therapeutic benefit from CBT (or GET) can be asserted. As it stands there is no reliable objective evidence for it, only highly problematic subjective evidence and interpretations, and grossly exaggerated claims. It certainly does not provide any primary explanatory or curative power.

Lines 363-366.
COMMENT: Agree.

Lines 367-403 (Conclusion section)
COMMENT: Generally I agree with this section, with a couple of specific comments.

Lines 378-380 (and 38-43). Retiring the Oxford criteria.
COMMENT: This is a welcome and long overdue step. The Oxford criteria have been a major confounding factor in the science and management of ME/CFS.

However, it must be pointed out that while the (draft) P2P report recommends the Oxford criteria be retired, it also uses studies based on that criteria, most notably the problematic PACE study, to inform the report.

Furthermore, at various points the report clearly rejects any primary psychogenic component to this disorder, yet it still recommends CBT and GET.

But if the studies based on the Oxford criteria are removed from consideration, there remains no significant body of evidence to argue for the routine use of CBT or GET (as based on the primary psychogenic model used in PACE, at least).

If one of the final recommendations of the P2P process is to retire the Oxford criteria, than other recommendations cannot be based on the results from studies

using the Oxford criteria (with the obvious exception of studies comparing different criteria).

Line 385.
COMMENT: I am guessing that many serious medical disorders use what might be broadly called multimodal therapy and management, with a mix of primary and palliative treatments. But what that means for ME/CFS is not clear.