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By Email

Dr. Carmen Mundaca-Shah
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Re: Institute of Medicine ME/CFS Definition Provisional Panelists

Dr. Mundaca-Shah:

I appreciate the opportunity to comment on the Provisional Panel.

The Contract Must Be Cancelled

Let me first state, as I have expressed previously, I strenuously protest the existence of this contract. As before, I am submitting comments to Institute of Medicine (hereinafter “IoM”) because, should the contract proceed, God forbid, I wish to attempt to mitigate the damage it will do to the science of ME and to patient health.

Please note that many, perhaps a majority, of patients who are aware of this contract are so opposed to it that they refuse to engage at all with IoM. Thus, if the true extent of opposition were voiced, it would be much greater than you currently hear.

The Following Group of Panelists is Qualified

As to the present panel, we have some very good experts here. I think the slate of 8 panelists (7 ME/CFS experts plus Dr. Ronald Davis) is quite good overall:

Lucinda Bateman, MD: Internal Medicine
Lily Chu, MD: Internal Medicine and Geriatrics
Betsy Keller, PhD: Metabolics
Nancy Klimas, MD: Immunology
Martin Lerner, MD: Infectious Disease
Benjamin Natelson, MD: Neurology
Peter Rowe, MD: Pediatrics
Ronald Davis, PhD: Biochemistry and Genomics

Why the Panel, if it is Formed, Must Consist Entirely of ME/CFS Experts (except for Dr. Davis)

However, if this panel proceeds, it *must* consist entirely of ME/CFS experts (except for Dr. Davis). Briefly, this is for several reasons including:

- (1) The Science of this disease is extraordinarily difficult to comprehend *in toto* for the following reasons:
 - (a) the disease itself is very complex;
 - (b) the science of the disease has been extremely underfunded;
 - (c) the science of the disease has been intentionally warped, most significantly by CDC, NIH and the Wessely School of ME/CFS psychiatry

It will be impossible for non-experts to master the science of this disease in the relatively short time-frame demanded;
- (2) The decades-long history of intentional malfeasance and nonfeasance in HHS' involvement in this disease, including developing the substandard Fukuda definition and the intentionally and patently invalid Reeves Criteria; this history renders patients and experts justifiably wary of any attempt by HHS to redefine this disease or cause it to be redefined (via this contract); We require an all-expert panel to have any confidence that HHS will not attempt to perniciously influence the process to arrive at an invalid definition;
- (3) Excuse my frankness, but IoM has had (reportedly high percentages of) panelists in the past and present who have failed to disclose relevant information such as conflicts of interest and bias; We need an all expert panel to ensure this is not the case here;
- (4) In the present contract there is not substantial evidence that these patterns of activity and inaction on the part of HHS and IoM have been remedied;
 - (a) HHS has refused to voluntarily make the contract public; HHS has also failed to produce the contract pursuant to three FOIA requests, the first of which was filed in late September; HHS has ignored the 50 experts, over 170 patient advocates and over 3,200 patients who have pleaded with HHS in the strongest terms to not contract with HHS and to immediately adopt the ME/CFS Canadian Consensus Criteria (CCC) and on and on;
 - (b) IoM has refused so far to voluntarily make the contract public, to cancel the contract, to provide an all-expert panel and to ensure that all relevant information about panelists is disclosed;
- (5) In order to define a disease, one must have either first-hand clinical experience

with many patients and/or a body of science available, based upon relatively *accurate existing definition(s)* which science is capable of reliably distinguishing the disease from healthy states and other illness states by means of laboratory (or clinical) signs. Because the only relatively accurate existing definitions are CCC and ICC, one must mainly rely on these definitions. The number of studies using CCC is quite small and there are no studies, to my knowledge using ICC. Therefor, at present, it is not quite possible to formulate a *practical clinical* definition which relies entirely on signs. Thus, first hand clinical experience is absolutely essential in defining this disease. Non-experts obviously do not have this experience;

- (6) It is likely that some of the non-experts will not be sufficiently confident of the inaccuracy of Fukuda, Oxford, Reeves and other invalid definitions to discount them in whole or in part, as appropriate. This will lead to consideration of studies which are highly inaccurate and thus result in a warped definition;
- (7) The majority (50) of experts in this disease have stated in writing in the strongest terms that this contract will result in an inaccurate definition because of IoM's insistence in placing non-experts on panels. Listen to the experts!
- (8) Since ME/CFS, as a practical matter and unlike other diseases, has no home in any one specialty, there are ME/CFS experts in every medical specialty from which IoM wishes to derive panelists. Thus IoM's wish for representation of a wide diversity of specialties can be achieved entirely with ME/CFS experts.

Particularly Bad Prospective Panelists

While it is necessary that all of the non-experts be replaced, other than Dr. Davis, let me now focus on the two worst known offenders: Margarita Alegria, PhD and Cynthia Mulrow, MD.

Margarita Alegria

Dr. Alegria fails to mention in the short bio she provided anything about ME/CFS or that she has spoken and written on Neurasthenia in several published journal articles. She asserts in one article that 'CFS' is a "Neurasthenia Spectrum Disorder," and that Neurasthenia is a psychiatric illness, specifically Somatization Disorder. She has also co-authored a paper on what she believes Somatization to be which definition is patently absurd. All of the central conclusions of the paper are also ludicrously illogical.

These two papers prove that, not only does she think CFS is psychiatric, but that she also has incredible difficulty thinking logically (which is a detriment being a scientist on our disease definition panel) especially about our disease, related issues and illness redefinition.

The paper on Neurasthenia¹ states that "further research is needed to examine the concordance of neurasthenia spectrum disorders (e.g., ICD-10 neurasthenia, CFS, CCMD-2 and CCMD-3 for neurasthenia) across non-clinical, population-based samples across cultural contexts [cf. 21, 23]." [Emphasis added]

For this proposition, the authors cite a Pune, India study² of neurasthenia spectrum disorders. The authors of that paper state in the abstract that: "Clinically significant fatigue or weakness is a common but understudied clinical problem in India... Alternative criteria sets used in different clinical contexts suggest a range of conditions constituting neurasthenia spectrum disorders (NSDs)... CFS, ICD-10 neurasthenia, DSM-IV draft criteria for neurasthenia, and CCMD-2 neurasthenia."

This study was an attempt to see if the four so-called "neurasthenia categories" mentioned, including CFS, were able to well define idiopathic chronic fatigue in India!

Alegria repeatedly characterizes Neurasthenia as a Psychiatric disorder. In the final line of her Neurasthenia paper, Alegria calls Neurasthenia a Somatoform disorder: "Significantly, our study is timely given the attention being paid to the classification of somatoform disorders and comorbidity, as well as on the role of culture and social factors on the epidemiology of such disorders."

Alegria has also written an article with a good number of extraordinarily illogical conclusions on Somatization.³ Since Alegria defines CFS as Somatization, this paper on somatization is extremely relevant.

Here are the 6 big problems I found with this paper. All six statements are absolutely ludicrous:

- (1) "Proposes the use of 3+ current General Physical Symptoms for designating a 'case'" of somatization;
- (2) claims their finding that "Medically Unexplained Physical Symptoms were not independently associated with psychopathology" logically leads one to their above conclusion (that 3 physical symptoms = somatization);
- (3) counts a physical symptom as being definitely "medically unexplained" if the patient said their doctor didn't mention the cause;
- (4) Says the fact that they found a high prevalence of physical symptoms (which were

¹ *Prevalence of Neurasthenia, Comorbidity, and Association with Impairment Among a Nationally Representative Sample of US Adults* (2012); <http://www.ncbi.nlm.nih.gov/pubmed/22349152>

² Paralikar V, Sarmukaddam S, Agashe M, Weiss MG (2007) *Diagnostic concordance of neurasthenia spectrum disorders in Pune, India*. Soc Psychiatry Psychiatr Epidemiol 42:561–572; <http://link.springer.com/article/10.1007/s00127-007-0196-x#page-1>

³ Whether medically unexplained or not, three or more concurrent somatic symptoms predict psychopathology and service use in community populations (2010); <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2905311/#!po=45.8333>

overwhelmingly 'medically explained') in the general population, "strongly supports the observation of many previous studies in the US and abroad that have shown that somatic symptoms represent a common expression of psychopathology..." (for the 'previous studies' they cite Wessely and Sharpe on CFS and the other "functional somatic syndromes" as being a single somatization disorder; <http://www.simonwessely.com/Downloads/Publications/CFS/108.pdf>)

- (5) Prominently concludes that "physical symptoms are an important component of common mental disorders" despite admitting in a much less prominent section that physical symptoms could well cause mental disorders and other alternative explanations exist for the co-occurrence of physical symptoms and mental disorders;
- (6) "Several investigators have suggested that it may be unnecessary to go through all the probes and procedures to rule out medical explanations given the stepwise association between somatic symptoms and common mental disorders such as anxiety and depression in primary care." In context, this statement seems to be saying that in studies of somatization, one should just assume that all physical symptoms in the general population are caused by mental disorders.

Alegria proposes that, any normal person with three physical symptoms, even if they are 'medically explained' be given the diagnosis of Somatization! (at least if you take what she says at face value and that is a reasonable interpretation because she doesn't qualify or add anything on to that statement; And also because the rest of this paper is such a train wreck of outlandish illogic, that interpretation of that statement would be right at home among the other extremes of ridiculousness).

But this is just so extreme that it's also possible, though unstated, that she thinks there should be additional criteria needed for a somatization diagnosis- I am guessing something like worrying about one's health, since she refers to Dimsdale and the DSM 5 revision process.

She says we should get away from qualitative criteria to dimensional criteria; what she means is that we should just count the number of physical symptoms and the more physical symptoms (even if medically explained!) the more likely the diagnosis of somatization.

She thinks the definition shouldn't be 'qualitative', which is nonsensical since the essence of a disease definition is qualitative; *a disease definition must describe the disease, not merely count up symptoms without more.*

She takes the old unsupported notion in psychiatry that the more symptoms one has, the more likely they are the product of somatization and pumps it up on steroids.

But then, she makes two more insane leaps of 'logic':

- (a) she says that since she found in this study that having symptoms that she characterized as "medically *unexplained*" didn't predict psychopathology *at all* compared to if one had symptoms that were "medically explained", she takes this to logically imply that *any* 3 physical symptoms, *even if they are medically explained* mean you are somaticizing.
- (b) then she takes the rule of thumb among psychiatrists that one should have, among other criteria, at least 5 physical symptoms to qualify for somatization and cuts it down to just 3 symptoms.

She justifies this by citing her results that show that one is likely to have *fewer* psychological problems if one has 5 physical symptoms than 3 physical symptoms!

Obviously, all of her findings in this study contradict her central theory, but she just finds jaw-dropping ways to incorporate them into that theory in stunning twists of illogic.

And then she goes even further through the looking glass with the other of the 6 head-smackers I outlined earlier.

All six of the above points made by Alegria are completely nonsensical and harmful statements about somatization and her attempt to redefine it. Not only does she write that CFS is a "Neurasthenia Spectrum Disorder," but that she also has incredible difficulty thinking logically especially about our disease, related issues and illness redefinition. Additionally, she failed to disclose that she has published (and spoken) on Neurasthenia (and "CFS").

Alegria absolutely must not be allowed anywhere near the definition of ME/CFS!

Cynthia Mulrow, MD

Dr. Mulrow didn't disclose that she had worked on CFS before, much less headed the official AHRQ (part of HHS) committee on CFS treatments! Nor did she disclose she used to work for Veterans' Affairs, which maintains a strongly anti-scientific and inaccurate stance on ME/CFS.

Mulrow, in the AHRQ report writes that Cognitive Behavioral Therapy (CBT) and Graded Exercise Therapy (GET) are the only effective therapies for ME; and that conclusion regarding GET is based entirely on studies based on the patently invalid Oxford definition of "CFS"! The Oxford definition, though it purports to define "CFS", defines nothing more than Idiopathic Chronic Fatigue since all it requires is 6 months of chronic fatigue without more. In her paper, she rated Oxford definition studies higher than Fukuda studies!

Mulrow is also an author of the IoM's 2011 report "Clinical Practice Guidelines

We Can Trust.”⁴ An August 2012 Rhode Island Medical Journal article concludes that Mulrow’s “IOM standards for the development of Clinical Practice Guidelines (CPGs) do not meet their own criteria of trustworthiness.”⁵ And neither does the present IoM ME/CFS redefinition process. Though the process has barely begun, it has already explicitly failed at least three of the eight IoM trustworthiness standards:

- (a) “Establishing Transparency: Guideline Development Groups’ methods should be detailed explicitly and publically available”;
- (b) “Management of Conflicts of Interest (COI): COI should be disclosed, discussed, divested”; and
- (c) “External Review; external review board should include all of: experts, organizations, federal agencies or an analogue, representatives of the public”

Fail! Mulrow must go!

With Whom to Replace the Non-experts

The proposed panel slate has no ME/CFS specific definitional experts, no cardiologists, no endocrinologists, only one infectious disease expert and not enough primary care practitioners/internists. Please remove all the non-experts except for Dr. Davis and replace with ME/CFS experts from these fields.

Psychologists and psychiatrists would be acceptable if, and only if, they were Prof. Leonard Jason, PhD, Gudrun Lange, PhD, Gordon Broderick, PhD, Alan Gurwitt, MD, Eleanor Stein, MD and Mady Hornig, MD.

I believe that any definitional panel would be incomplete without Prof. Jason as he has researched and written more extensively on ME/CFS definitions than anyone else. A second choice in that crucial area is Bruce Carruthers, MD.

The other indispensable field is that of Primary Care/ Internal Medicine, which is also underrepresented. The two indispensable panelists in this central field are Daniel Peterson, MD and Paul Cheney, MD.

I have listed relevant specialty areas with suggested panelists ranked within categories in descending order of expertise and value to the panel.

Developing Definitions

- (1) Leonard Jason, PhD
- (2) Bruce Carruthers, MD
- (3) Byron Hyde, MD

⁴ <http://www.iom.edu/~/media/Files/Report%20Files/2011/Clinical-Practice-Guidelines-We-Can-Trust/Clinical%20Practice%20Guidelines%202011%20Report%20Brief.pdf>

⁵ <http://www.rimed.org/rimedicaljournal/2013-08/2013-08-13-iom.pdf>

Primary Care/ Internal Medicine

- (1) Daniel Peterson, MD
- (1) Paul Cheney, MD, PhD
- (3) Derek Enlander, MD
- (3) Kenneth de Meirleir, MD, PhD
- (5) David Bell, MD
- (6) Susan Levine, MD

Epidemiology

- (1) Leonard Jason, PhD
- (2) Kenneth Friedman, PhD

Infectious Disease

- (1) John Chia, MD
- (1) Jose Montoya, MD
- (3) Mady Hornig, MD, MA
- (3) Ian Lipkin, PhD
- (5) Dharam Ablashi, DVM

Cardiology

Martin Pall, PhD

Psychiatry/ Psychology

- (1) Leonard Jason, PhD
- (2) Eleanor Stein, MD
- (2) Gudrun Lange, PhD
- (2) Gordon Broderick, PhD
- (5) Alan Gurwitt, MD
- (5) Mady Hornig, MD

Health Care Education

- (1) Kenneth Friedman, PhD
- (2) Gailen Marshall, MD

Prospective Panelists' Non-Disclosure Must be Remedied

I am concerned that Drs. Alegria and Mulrow failed to disclose highly relevant information which shows them to be unable to objectively and logically define ME/CFS. I am also concerned that there may well be other prospective panelists who have failed to disclose relevant information.

You may be aware that according to a 2006 report of the Center for Science in the Public Interest,⁶ “the National Academies of Science (NAS) does not appear to consider

⁶ Center for Science in the Public Interest, *Ensuring Objectivity and Independence at the National Academies* (2006);

information about potential bias or conflicts of interest prior to nominating individuals to a committee. As a result, about half the panels examined had scientists with identifiable biases who were not offset by scientists with alternative points of view...

“The NAS has allowed numerous scientists (and others) with blatant conflicts of interest to sit on committees. Compounding that problem, those conflicts of interest usually are not disclosed to the public...

“Nearly one out of every five scientists appointed to an NAS panel has direct financial ties to companies or industry groups with a direct stake in the outcome of that study. This consistent pattern of appointing scientists with conflicts of interest clearly violates the spirit of the Federal Advisory Committee Act amendments that apply to NAS...

And “biographies are woefully inadequate because, in a majority of cases, they fail to provide crucial data regarding conflicts of interest and points of view.

IoM is quite assertive in prominently and unequivocally declaring that its “consensus studies are conducted by committees carefully composed to ensure the requisite expertise and to avoid conflicts of interest.”⁷

Imagine my surprise and dismay, when looking into IoM’s current Gulf War Illness/ “Chronic Multi-Symptom Illness” redefinition group I discovered numerous significant undisclosed conflicts of interests, biases and an extreme overall lack of balance to the committee.⁸

In light of the above, I am quite concerned that there may well be additional undisclosed relevant information about proposed panelists. Thus I am requesting in the strongest terms that:

- (a) you please tell me, in a timely fashion, what IoM’s policy or instructions to panelists about providing bios and disclosing relevant information, if any, are. Please provide all details; and
- (b) you please make crystal clear to each prospective panelist, in writing, that all relevant information absolutely *must* be disclosed to the public and that you keep the public updated on these efforts and provided with copies of all written correspondence with panelists on the subject.

The burden of discovering previous work done on the disease and related illnesses, conflicts of interest, biases and any other relevant information should not fall on the shoulders of extremely disabled patients. Uncovering this information takes a huge amount of work and is impossible unless one has free access to medical journals, which is

<http://cspinet.org/new/pdf/nasreport.pdf>

⁷ IoM website; <http://www.iom.edu/About-IOM/Study-Process.aspx>

⁸ Reilly, Justin, *Composition of IoM GWI/CMI redefinition panel: It Ain't Pretty*; on Phoenix Rising ME/CFS internet forums; <http://forums.phoenixrising.me/index.php?threads/composition-of-iom-gwi-cmi-redefinition-panel-it-aint-pretty.26553/>

rare for patients to have. Additionally, relevant information may well be missed by patients, despite the huge effort made.

The panelists already know if there is relevant information, what it is and where exactly it is. Efficiency and fairness demand that panelist be duly diligent in providing relevant information.

In summary, this contract must be cancelled. But in the case that it is not, all of the non-experts (except Dr. Davis) must be replaced with ME/CFS experts. Particularly troubling non-experts are Drs. Alegria and Mulrow. Finally, please take the suggested steps to ensure all relevant information is disclosed by panelists.

Thank you for your consideration.

Sincerely,

/S/

Justin Reilly, esq.