Public Comment for the January 13, 2015 CFSAC Meeting
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The utter folly of choosing inexperienced non-experts outside the field to write about a contested disease is shown in the opening statement of the 2014 Pathways to Prevention Workshop (P2P) on "Myalgic Encephalomyelitis/Chronic Fatigue Syndrome" Draft Executive Summary:

> *Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, complex, multi-faceted condition characterized by extreme fatigue and other symptoms that are not improved by rest. The etiology and pathogenesis remain unknown; there are no laboratory diagnostic tests; and there are no known cures.*

In the first place, it is entirely unclear what the P2P draft report is about. It purports to be about a condition "characterized by extreme fatigue." However, the neurological disease myalgic encephalomyelitis (ME) is NOT characterized by extreme fatigue. Unexplained fatigue is the characteristic feature of chronic fatigue syndrome (CFS), not myalgic encephalomyelitis (ME). Classic descriptions of the neurological disease ME [Acheson, 1959; Ramsay, 1986] and the 2011 ME International Consensus Criteria (ICC) [Carruthers, 2011] do NOT list fatigue as a diagnostic symptom of the disease – let alone as a characteristic feature of the disease. Therefore, the P2P draft report cannot be about ME. However, the novice authors of the report seem to be unaware this fact and wish to include ME as a part of the undefined condition they are referring to as "ME/CFS" that is "characterized by extreme fatigue."

This in the complete 1986 definition of myalgic encephalomyelitis by Dr. A. Melvin Ramsay written after 30 years of carefully observing the disease in hundreds of patients:

> *A syndrome initiated by a virus infection, commonly in the form of a respiratory or gastrointestinal illness with significant headache, malaise and dizziness sometimes accompanied by lymphadenopathy or rash. Insidious or more dramatic onsets following neurological, cardiac or endocrine disability are also recognised. Characteristic features include:*
>
> *(1) A multisystem disease, primarily neurological with variable involvement of liver, cardiac and skeletal muscle, lymphoid and endocrine organs.*

(2) Neurological disturbance – an unpredictable state of central nervous system exhaustion following mental or physical exertion which may be delayed and require several days for recovery; an unique neuro-endocrine profile which differs from depression in that the hypothalamic/pituitary/adrenal response to stress is deficient; dysfunction of the autonomic and sensory nervous systems; cognitive problems.

(3) Musculo-skeletal dysfunction in a proportion of patients (related to sensory disturbance or to the late metabolic and auto immune effects of infection).

(4) A characteristically chronic relapsing course. [Ramsay, 1986]

Where's the "extreme fatigue" that the inexperienced P2P authors claim characterizes "ME/CFS"? **It should be clear that whatever "ME/CFS" is in the P2P draft report, it is not ME**. Consistent with Ramsay's classic definition of ME, the 26 highly qualified and experienced professionals who developed the 2011 International Consensus Criteria document, published in the Journal of Internal Medicine, also do NOT include fatigue in the name of the disease or as a criterion for making an ME diagnosis. They state:

Using 'fatigue' as a name of a disease gives it exclusive emphasis and has been the most confusing and misused criterion. No other fatiguing disease has 'chronic fatigue' attached to its name – e.g. cancer/chronic fatigue, multiple sclerosis/chronic fatigue – except ME/CFS. Fatigue in other conditions is usually proportional to effort or duration with a quick recovery and will recur to the same extent with the same effort or duration that same or next day. The pathological low threshold of fatigability of ME described in the following criteria often occurs with minimal physical or mental exertion and with reduced ability to undertake the same activity within the same or several days.

The ICC document states ME is characterized by an abnormal biological response to exertion or exercise that is objectively measurable by the 2-day cardiopulmonary exercise test (CPET). [Carruthers, 2011; VanNess, 2007] According to the ICC, "Pain and fatigue are crucial bioalarm signals that instruct patients to modify what they are doing in order to protect the body and prevent further damage." The fatigue experienced by ME patients is the result of an underlying disease process and cannot be considered as medically unexplained any more than can be the fatigue experienced by cancer and MS patients.

Why then would the P2P draft report authors include the "ME" part of the term "ME/CFS" that is used apparently to refer to some condition other than ME? The only reason can be because bureaucrats at the Department of Health and Human Services (HHS) told the compliant members of the "unbiased, independent" P2P panel to use the term "ME/CFS" throughout their report and never mind what it means. The only published case definition using the term "ME/CFS" is the 2003 Canadian Consensus Criteria (CCC) document [Carruthers, 2003], but confusingly the P2P draft report uses "ME/CFS" in a broader sense to refer to some nebulous fatigue condition that is never delineated.

The hybrid term "ME/CFS" explicitly embodies what has been the major problem in the field ever since the CDC dispatched two inexperienced, unqualified investigators to the Lake Tahoe region of Nevada in the fall of 1985 in response to one of the many outbreaks of ME in the 20th century – the conflation of the neurological disease ME with a poorly described, socially constructed syndrome based almost entirely on the unmeasurable, undefinable symptom of perceived fatigue.

For 26 years after the CDC mischaracterized ME as a fatigue syndrome in 1988, [Holmes, 1988] all patients with ME in the US have been misdiagnosed as part of the CDC's overly broad chronic fatigue syndrome collection of self-reported symptoms. Simply tacking the term "ME" on to "CFS" using a slash does absolutely nothing to correct this problem. In fact, using "ME/CFS" makes the problem much worse. How can the neurological disease ME ever be separated from the fatigue condition CFS if the two disparate terms are combined in a single term? Of course they can't be separated. This is why HHS now favors the unclassifiable, undefined term "ME/CFS" and has instructed their "unbiased, independent" P2P panel to use "ME/CFS" exclusively in their report to refer to who knows what.

If any of the P2P draft report authors had ever attempted to diagnose a patient with "ME/CFS" and consulted the current US ICD-9-CM, used to code diagnoses for billing and reporting purposes, they would find that the hybrid term "ME/CFS" is not listed. Only the diagnostic term "chronic fatigue syndrome" is listed as 780.71 under "Symptoms, Signs, And Ill-Defined Conditions."

"ME/CFS" also has never been listed in the World Health Organization's International Classification of Diseases (ICD). ME, however, has been listed in the WHO ICD as a neurological disease since 1969. Indeed, the hybrid "ME/CFS"

diagnostic term can never be legitimately listed in the WHO ICD. It's an unclassifiable chimera that violates the WHO rule of only using mutually exclusive diagnostic terms that fall within a single category.

Nor will the hybrid term "ME/CFS" be listed in the upcoming US ICD-10-CM, official October 1, 2015. Only the diagnostic terms "chronic fatigue syndrome" in the general symptoms section and "benign myalgic encephalomyelitis" in the neurological diseases section will be listed. How then will a doctor code an "ME/CFS" diagnosis? Because doctors in the US have only been informed about CFS, if informed at all, and know nothing of ME, "ME/CFS" will be coded as the ill-defined condition CFS and not as the neurological disease ME. This fact renders HHS's current use of the term "ME/CFS" hypocritical and nonsensical.

How then is one to interpret such statements in the P2P draft report as, "Patients experience stigma from the diagnosis of ME/CFS, including social isolation and judgment"? How can patients experience stigma from a diagnosis of "ME/CFS" when CFS is the diagnostic term now used by doctors in the US? The draft report is retrospectively calling CFS "ME/CFS." This muddled historical revisionism is the result of the "unbiased, independent" P2P panel allowing itself to be misguided by HHS bureaucrats.

Despite obviously not knowing what "ME/CFS" might be, the P2P draft report authors on page 3 make the breathtaking leap of faith to assure readers that "ME/CFS exists." This is bit like declaring Bigfoot exists despite being unable to come up with a clear description of the creature. However, the confusion of the authors is understandable because their newly acquired knowledge of "ME/CFS" is largely based on a recent Agency for Healthcare Research and Quality (AHRQ) Evidence Report No. 219 "Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome" [Smith, 2014] also written by "unbiased, independent" neophytes in the field.

The Executive Summary of the AHRQ Final Evidence Report on page ES-1 makes the egregious misstatement that of the eight published case definitions considered, "**All include persistent fatigue not attributable to a known underlying medical condition**, **as well as additional clinical signs and symptoms.**"

Evidently, the "unbiased, independent" authors of the AHRQ report Executive Summary in their eagerness to make "ME/CFS" all about "persistent fatigue" failed to note that several pages later, the main report states, "***All but one*** **of the definitions include persistent fatigue not attributable to a known underlying**

medical condition, as well as additional clinical signs and symptoms that do not all need to be present to establish the diagnosis." [Smith, 2014, page 2, italics added]

Table 2 on page 14 of the AHRQ Evidence Report clearly shows that the one exception that does not use the criterion of fatigue in its case definition is the "International ME Carruthers 2011" case definition in the fourth column from the left. [Carruthers, 2011]

This omission is vitally important because the neurological disease ME is not a fatigue syndrome, nor a part of any fatigue syndrome. Nevertheless, HHS and their Centers for Disease Control (CDC) have failed to recognize the disease and to list ME as an exclusionary diagnosis for inclusion in the CDC's broad chronic fatigue syndrome umbrella diagnostic category.

It can be argued, supported by extensive research, that ME itself is a "known underlying medical condition" to which any fatigue reported by a patient can be attributed. Therefore, ME cannot be considered part of any condition characterized be unexplained fatigue – including ironically HHS's new undefined "ME/CFS" fatigue illness blend.

It has been the long-standing policy of HHS to support the misdiagnosis of ME patients with CFS – a policy that spares the private insurance industry the cost of appropriately medically testing for and treating ME. Keeping ME concealed within CFS, and now "ME/CFS," also spares the Department of Health and Human Services the expense of appropriately funding biomedical research on a major neurological disease. Instead, HHS now gets away with only spending a pittance each year on often social science research of an elusive fatigue condition called CFS.

HHS wishes to avoid at all costs acknowledging their concealment of ME for decades within CFS. Apparently the "unbiased, independent" P2P report authors are happy to oblige HHS by failing to read any further than the Executive Summary of the AHRQ report and using HHS's new undefined, catch-all term "ME/CFS" without question.

The P2P authors naively misrepresent ME in their draft report as a part of a dazzling "complex, multi-faceted condition characterized by extreme fatigue" completely oblivious to the history of ME in the medical literature and its current 2011 ICC case definition. Anyone familiar with the field would have noticed the

glaring error on page ES-1 of the AHRQ Evidence Review and pointed it out rather than repeating it.

If the P2P draft report authors had read the 2012 ME International Consensus Primer (IC Primer or ICP) [Carruthers. 2012], they would know better than to parrot the CDC's popular myth that "there are no laboratory diagnostic tests" for the disease. **The IC Primer already lists over 30 laboratory tests and imaging studies specifically useful in diagnosing ME, in addition to standard laboratory screening tests.**

Despite the P2P draft report's familiar call that more research is needed, it is completely unclear just what it is that needs to be researched. Research on any actual disease has been hampered for decades by use of the overly broad 1994 Fukuda CFS case definition. [Fukuda, 1994] Fukuda CFS research results cannot be applied to any specific patient group or consistently replicated.

The P2P draft report completely fails to address the total lack of funding by the National Institutes of Health (NIH) for any research on the neurological disease ME with subjects selected using specific ME criteria. As the IC Primer states, **"There is a current, urgent need for ME research using patients who actually have ME." This urgent need is completely ignored by the authors P2P draft report who were charged with identifying "research gaps and future research priorities."**

The P2P draft report calls for the 1991 Oxford CFS definition to be "retired." No mention is made, however, of retiring the CDC's 1994 CFS Fukuda definition which has also been impairing progress in the field for over 20 years. Does "retiring" the Oxford definition mean the CDC will remove the 2011 PACE trial, which used the Oxford definition, as a reference in their CFS continuing medical education course? The CDC has used the Oxford-based PACE trial to support their irresponsible recommendation of using exercise as "therapy"to treat CFS.

In fact, "retiring" the Oxford definition means very little in actual practice because Oxford has never been used in NIH-funded CFS research. Will the invalid UK PACE trial be retracted based on the P2P panel's recommendation? It won't be. No doubt, the CDC will continue to used Oxford-based research as a reference whenever it supports the CDC's agenda of recommending primarily behavioral treatments for their chronic fatigue syndrome.

Unbelievably, to remedy the current chaos caused the use of multiple case definitions, the P2P draft report authors want to "assemble a team of stakeholders (e.g., patients, clinicians, researchers, federal agencies) to reach consensus on the definition and parameters of ME/CFS." Apparently, the draft report authors are unaware that a consensus of truly independent, expert professionals in the field was reached over 10 years ago in the 2003 Canadian Consensus Criteria (CCC) and updated in 2011 by the International Consensus Criteria (ICC). The ICC have now been used to select subjects with ME for research studies indicating widespread neuroinflammation and immune system abnormalities are associated with the disease. [Nakatomi, 2014; Brenu, 2013]

However, when then HHS Secretary Kathleen Sebelius was offered the opportunity in 2013 of adopting the compromise CCC case definition as recommended by 50 expert professionals in the field, she summarily rejected the proposal. Instead, HHS is now pursuing a new unneeded redefinition of "ME/CFS" using a contracted Institute of Medicine panel composed mostly of the controllable "unbiased, independent" non-experts favored by HHS bureaucrats.

Nevertheless, the unknowledgeable P2P panel is calling for yet another grand consensus by a "team of stakeholders" and a pie-in-the-sky "national and international research network." **It should be clear to anyone that the problem is bad faith at HHS, not the lack of existing excellent consensus diagnostic and treatment guidelines that can also be used for research.**

The diagnostic and research criteria for other major diseases are developed by expert professionals in the field and their organizations without inference by government bureaucrats and agencies. The harm caused by governmental meddling with disease criteria is demonstrated by the unscientific 1994 Fukuda CFS criteria controlled and developed primarily by NIH and CDC bureaucrats with major input from UK psychiatrists. These bureaucrats had personal and institutional agendas which they placed above the public interest. [Straus, undated] For two decades the overly broad Fukuda CFS criteria have confounded research and led to the medical neglect and mistreatment of patients.

ME expert Dr. Byron Hyde wisely observed in a paper presented in New South Wales in 1998:

> *Definitions are not diseases, they are often simply the best descriptions that physicians and researchers can offer, with their always imperfect knowledge, to describe a disease. Good definitions are good because they*

> *correspond closely to the disease state being described. It is thus important that those that attempt to define any disease or illness to have long term clinical experience with patients with this illness.* ***There is simply no place for the bureaucrat in defining illness.*** *All definition of epidemic or infectious illness must be based upon persistent clinical examination of the afflicted patient, an understanding and exploration of the environmental factors producing that illness, and pathophysiological examination of tissue from those patients. For similar reasons, I believe that the inclusion of psychiatrists in the defining of an epidemic and obviously disease of infectious origin, simply muddies the water for any serious understanding of that disease.* [Hyde, 1998. Emphasis added]

Yet the naive P2P panel is calling for still more governmental interference in medical science by wanting "federal agencies" to be included in choosing yet another set of criteria for a fatigue condition now called "ME/CFS." **When will professionals realize the harm caused by governmental interference with science and refuse to take part in such efforts?** Currently, the only two contemporary case definitions that reflect the physical reality of the disease were developed by professionals in the field with a minimum of of governmental interference – the 2003 CCC and 2011 ICC.

The unknowledgeable P2P panel from outside the field seems to be unaware that most of the problems the panel has "discovered" have already been addressed by the 2011 ICC and 2012 IC Primer. HHS can begin correcting these problems by recognizing ME as the distinct neurological disease that it is and removing ME from the broader inappropriate CFS category, as called for by the ICC. **HHS needs to assume an ancillary role and begin disseminating the IC Primer to doctors so they can make the differential diagnosis of ME, instead of continuing to place ME patients at risk by misdiagnosing them with CFS or some new "ME/CFS" pseudo-diagnosis.**

The tools for educating medical professionals about ME already exists in the ICC and IC Primer. **The problem is HHS does not want to devote the necessary resources to educating doctors and healthcare professionals on how to recognize, diagnose, and properly treat ME. HHS prefers, instead, to accept the increased disability in the US population and increased yearly cost to the economy caused by medically neglecting and mistreating ME**. The HHS leadership has chosen to support the bureaucrats at the CDC's inept CFS program, and their negligent CFS Toolkit collection of dangerous medical misinformation, over the public interest. [CDC, undated]

Why would HHS ever implement any of the grand proposals of the P2P draft report when HHS stubbornly refuses to take even the low-cost, simple step of removing the harmful, inaccurate CFS Toolkit from the CDC website and disseminating the excellent IC Primer to healthcare professionals? Doctors now are unaware of the possible permanent harm to their ME patients posed by exercise and overexertion. ME must be recognized and diagnosed early so the patient can be advised to take total rest to limit the risk of permanent severe disability caused by the disease. Pioneer ME doctor A. Melvin Ramsay has noted:

> *The clinical picture of myalgic encephalomyelitis has much in common with that of multiple sclerosis but, unlike the latter, the disease is not progressive and the prognosis should therefore be relatively good. However, this is largely dependent on the management of the patient in the early stages of the illness.* ***Those who are given complete rest from the onset do well...*** [Emphasis added]

Doctors have been left totally uninformed about ME by the continued misconduct of HHS bureaucrats. Instead of conducting seminars educating doctors about ME with information that is now readily available, HHS is squandering public money on the obfuscating P2P Workshop and its report which will soon be forgotten. **The leadership at HHS has chosen to place their highest priority on protecting the mistakes of their bureaucrats and the profits of the insurance industry rather than protecting the public health.**

The primary consideration of "unbiased, independent" P2P draft report is obviously pleasing the HHS bureaucrats who commissioned the report rather than adding any clarity to the muddled mess created by those very bureaucrats. Any useful suggestions made in the final P2P report will simply be ignored by HHS bureaucrats as they have done for decades. **The P2P draft report can hardly be expected to address the main problem currently forestalling any hope of progress in researching, diagnosing, and treating ME – the refusal of HHS to listen to the truly independent and knowledgeable medical and scientific professionals in the field**. Instead, HHS continues to enlist controllable non-experts to add more confusion and delay to the field. The P2P draft report itself is a prime example.

Further reasons for disseminating the 2012 International Consensus Primer now to healthcare personnel and the medical risks to myalgic encephalitis patients posed by continued misdiagnosis with chronic fatigue syndrome are given in my December 17, 2014 article: Why There Is an Urgent Need to Widely Distribute the Myalgic Encephalomyelitis International Consensus Primer to Doctors. https://drive.google.com/file/d/0B4uD-VyWmIw2T3Y2NTNLWjRBeFE/view?usp=sharing

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