IACFS/ME
International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis
Dedicated to research, education, treatment and finding a cure for
Chronic Fatigue Syndrome/Myalgic Encephalomyelitis

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Dear Japan ME Association:

We provide this letter in response to your request for our comment on the "ME/CFS Treatment Guidelines for Japan (Draft)," which we understand is currently being re-evaluated. We have reviewed the English translation of sections that you sent to us which were of the most concern to your patient association.

The International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis is concerned about **the potential harmful impact of this document on ME/CFS patients in Japan**, particularly as policymakers, government officials, medical researchers, and healthcare providers are often unfamiliar with the symptoms and complex nature of ME/CFS.

As noted in our "Chronic fatigue syndrome/ myalgic encephalomyelitis primer for clinical practitioners: 2014 edition," (1) ME/CFS is a serious and complex physical illness with neurological, immunological, endocrinological, autonomic, energy metabolism, and other physiological abnormalities. These abnormalities were also documented in a 2015 review (2) of over 9,000+ studies by the US National Academy of Medicine. It is not a psychiatric or psychological disorder.

Patients suffer from substantially impaired physical and/or cognitive functioning due to severe fatigue, widespread musculoskeletal and joint pain, memory and concentration problems, unrefreshing sleep, autonomic dysfunction, and flu-like symptoms. A key feature of the illness is post-exertional malaise (PEM), a worsening of symptoms following even minimal physical or cognitive exertion. The severity and duration of PEM is often disproportionate to the precipitating activity. For example, a short shopping trip might land a patient in bed for days.

The World Health Organization currently classifies myalgic encephalomyelitis as a disease of the central nervous system (G93.3) (1).

It is of concern to us that ME/CFS Treatment Guidelines for Japan (Draft) discusses Graded Exercise Therapy as a recommended treatment for ME/CFS. GET studies suffer from multiple flaws including overly broad inclusion criteria, a paucity of objective outcome measures, questionable blinding of participants, high trial participant drop-out rates, post-hoc modifications of outcome measures, selective outcome reporting, and poor reporting of harms.

In 2016, the United States Agency for Healthcare Research and Quality (3) rated the evidence for GET as "Insufficient" and recommended that the broad "Oxford" criteria used for many GET studies be retired due to its non-specific nature. And in 2017, a re-analysis of the United Kingdom (4) multi-million-pound PACE trial using the original outcome measures found that recovery rate with GET fell from an initially reported 22% to 4% and was not statistically significant from the recovery rate of 3% reported with usual medical care. Consequently, we are skeptical about the validity of GET trial results. The US Centers for Disease Control and Prevention came to similar conclusions in the Fall of 2017 and are currently in the process of removing GET as a recommended treatment for ME/CFS (5).

Moreover, evidence against GET exists. Our organization does not recommend GET because our clinician members, who have taken care of ME/CFS patients for decades, tell us it does not work. Surveys of thousands of patients, across different countries, over many years, and conducted by different groups consistently find that very few benefit substantially from GET. Instead, a mean of 50% (6) of respondents disclosed that their health worsened with GET. Finally, physiological studies support patient and clinician accounts. For example, some studies suggest that patients have an impaired aerobic energy (7) system while others demonstrate an abnormal immunological response (8) to exercise. (Interestingly, the discussion sections of published GET studies rarely address this contrary evidence.) Thus, we hope that GET will not be recommended in the final version of the document.

Further, we share your concern that because the ME/CFS Treatment Guidelines (Draft) frames behavioral approaches such as CBT, yoga, and drug treatments such as antidepressants as blanket treatments for ME/CFS, **the document may reinforce erroneous beliefs among healthcare providers that ME/CFS itself is a psychological or psychogenic illness that can be cured or reversed by such interventions**. Accordingly, we believe the document should prevent any such misunderstandings by:

a) making it explicitly clear that ME/CFS is not a psychological or psychogenic illness,
b) conveying that these treatments are merely supportive and not primary, curative, or disease-modifying, treatments, and should be incorporated in a similar matter as they are for other medical conditions like cancer, heart disease, etc. (e.g., cancer patients would never be solely treated with CBT or yoga),

c) emphasizing that such treatments are not mandatory for all ME/CFS patients (e.g., a patient who does not have depression as a comorbidity (depression is not a symptom of ME/CFS) should not be given antidepressants).

We hope these comments are helpful to you, the research committee, and the government agencies reviewing the Draft in producing a scientifically accurate guideline that benefits everyone.

Sincerely,

Fred Friedberg, PhD and Lily Chu, MD, MSHS on behalf of the

The International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis Board

www.iacfsme.org

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