March 19, 2023

Dr. Eldrin Lewis
Co-chair
RECOVER Clinical Trials Steering Committee

Dear Dr. Lewis,

We have not received a response to our February 28th letter regarding RECOVER's plans to conduct a clinical treatment trial of exercise therapy in people with Long COVID. We are following up to underscore our concerns about the safety and efficacy of this clinical trial. Thus far RECOVER has provided no information to the public about the justification for the study or how it will be designed.

People with Long COVID who meet the criteria for myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) and those with post-exertional malaise (PEM) must be excluded from this study. There is no justification for using exercise therapies designed for patients who do not have ME/CFS or PEM on a Long COVID population with ME/CFS or PEM.

Attached is a summary of ME/CFS studies to date that provide objective evidence of an abnormal response to exercise across multiple bodily systems and functions including: immune, neurological, and cardiovascular/autonomic systems, metabolism and the microbiome. This evidence also includes objective measures of impairment in exercise capacity that cannot be attributed to deconditioning.

The breadth and volume of the objective evidence of an abnormal response to exercise in people with ME/CFS and PEM is distinctive and robust. Too often, researchers who employ exercise interventions for rehabilitation lack awareness and understanding of this evidence.

These findings should inform all aspects of study design for RECOVER's planned clinical trial of exercise therapy for Long COVID. RECOVER cannot afford to ignore this evidence given that up to half of those with Long COVID meet the diagnostic criteria for ME/CFS, and PEM is experienced by the majority of those with Long COVID.

If this trial moves forward we need to know that:

1. Long COVID participants who meet the diagnostic criteria for ME/CFS or who report PEM will be excluded from this study,
2. Participants will be screened for PEM at the outset of the study and assessed for PEM after every exercise intervention using a validated instrument.
3. PEM will be included in the study's harms reporting and informed consent, and
4. The study's conclusions will be carefully limited to the specific cohort studied and not generalized as appropriate for all Long COVID patients, including those with PEM.

Sincerely,

Ben HsuBorger
U.S. Advocacy Director
#MEAction

CC:
RECOVER Clinical Science Core,
Dr. Walter Koroshetz, MD, Director, National Institute of Neurological Disorders and Stroke
Dr. Gary Gibbons, Director, National Heart, Lung, and Blood Institute
Dr. Hugh Auchincloss, Acting Head of National Institute of Allergy and Infectious Diseases
Dr. Joseph Breen, Immunoregulation Section Chief, NIAID
RADM Michael Iademarco, Deputy Assistant Secretary for Science and Medicine, Office of the Assistant Secretary of Health, HHS