

Executive Summary: #MEAction Response to CDC Draft Systematic Evidence Review for Management of ME/CFS

We find the conclusions of the CDC 2020 draft systematic review on the treatment of myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) to be fundamentally flawed, and we strongly urge that this review not be published. We focus on the review of Graded Exercise Therapy (GET) and Cognitive Behavioral Therapy (CBT) treatments, which have the potential to do the most harm to people with ME/CFS. Our critique covers four key topic areas:

Applicability of Findings. The GET and CBT studies that undergird the review do not apply to people with ME/CFS as defined by CDC, as they do not require post-exertional malaise (PEM), identified as one of the three core symptoms of ME/CFS by CDC. These studies' patient inclusion criteria employed older case definitions—primarily Oxford and Fukuda—that are overly inclusive and create significant patient population heterogeneity. These studies' findings are from populations that do not have a direct relationship to people with ME/CFS as defined by the CDC.

Risk of Bias. The significant risk of bias in this review calls the validity and reliability of its conclusions into question. Based on best available guidance in the field of systematic reviews, the included CBT and GET studies should be assigned a “high” risk of bias, primarily because neither patients nor clinicians were blinded to their intervention group, and the trials relied on subjective primary outcomes. These low quality study designs create risk of patient response bias and provider preference bias that overestimate purported treatment benefits. The reported subjective improvements in these studies are often not supported by objective findings.

Exclusion of Harms Evidence. This review failed to adequately address potential harms from GET and CBT “treatments” for people with ME/CFS. It covered only the inadequate reporting available in the included randomized controlled trials. The review excluded numerous observational studies that present physiological evidence of exercise intolerance in people with ME/CFS, as well as surveys involving thousands of patients that reported harms from GET and CBT. Rigid inclusion/exclusion criteria in this area is not aligned with AHRQ and AMSTAR II best practice. Other ME/CFS reviews were more robust in their investigations of adverse events.

Interpretations of Results. This review's meta-analyses were misleading due to high risk of bias, high heterogeneity, and low strength of evidence. Conclusions drawn from the average of small, subjective improvements—which often disappear by post-intervention follow-up and which are not supported by objective improvements—are not meaningful for ME/CFS patients' ultimate health and well-being. Subgroup analyses do not inform the authors' interpretations of results as they should, nor do they adequately address underlying concerns regarding the utility of reported “average effects.”

Publication of this review will lead to confusion about the appropriate treatment for people diagnosed with ME/CFS as CDC defines it. Clinicians will prescribe GET and CBT, believing they are executing the best, evidence-based practice, unaware that they may be putting their already vulnerable patients at risk of harm. It is imperative that this fundamentally flawed review not be published.