

Subject: Responses to public comments on the Multi-Site Clinical Assessment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (MCAM) study (Federal Register Docket No. CDC-2020-86)

1. Data harmonization is critical.

Because of the high degree of heterogeneity associated with ME/CFS, we need the largest possible data set to better understand it. By aligning as many data fields as possible across different studies, we create the opportunity to combine data sets across organizations. We encourage CDC to streamline the data collection process by reducing the number of instruments administered to accommodate the limited capacity of many individuals with ME/CFS. We also suggest that the CDC align the instruments used in the MCAM study with those most commonly used by those in the community, as outlined in Appendix A. While we acknowledge that 100% data harmonization is impossible, aligning on a majority of the data fields captured is important, and will only serve to accelerate our understanding of this disease.

Response: Data harmonization is critical to advance ME/CFS research. One of the most important objectives of the MCAM study was to use standardized data collection instruments/forms to measure common data elements or illness domains of ME/CFS over time. The CDC ME/CFS research team developed the standardized protocols for the four components of the MCAM study. These protocols were further refined by the MCAM site investigators based on their commonly used instruments and clinical practice routine at their sites. The MCAM protocols have covered numerous standardized instruments listed in the Appendix that you shared. Additionally, the early stage of the MCAM study provided evidence to support the 2015 IOM report on ME/CFS and the recommendations from the 2019 NINDS/CDC Common Data Elements (CDE) project. After the CDE project, we incorporated additional assessment tools recommended by the CDE Project. Since the MCAM study is an ongoing longitudinal study that began in 2012, for comparable outcome measures over time we cannot add or change instruments at this point. However, in future studies we will absolutely consider additional instruments to enhance data harmonization.

2. Use of a centralized GUID system is essential.

The NIH National Institute of Neurological Diseases and Stroke (NINDS) has created a mechanism to assign study participants with a global unique identifier (GUID) that allows them to be tracked across several studies. This GUID tool can be easily integrated into the data capture process to generate GUIDs, without exposing personally-identifiable information (PII) or protected health information (PHI). The ability to match GUIDs for individuals who have participated in multiple studies will create a mechanism to aggregate data and gather a more holistic and longitudinal understanding of an individual's disease history. The GUID is embedded into the You + ME Registry, so by including it in the MCAM study, we will be able to understand if participants in the MCAM study are also tracking data in the Registry and create a mechanism to facilitate the sharing of data.

Response: As mentioned before, our study is ongoing and in its inception we did not obtain consent from study participants for the use of GUID. Although we cannot reconsent for this study, we understand the benefits you described and will use QUID in future studies.

3. Ongoing data capture is illuminating.

One of the insights we gleaned from the community in the development of You + ME was the need to capture a moving picture of the illness over time, versus a snapshot at a single time point. To meet this need, and to empower individuals living with ME/CFS with information about their disease, we created a symptom tracking app. The app has been well received by the community with users on average logging data on 88% of the available tracking days (the default is set to every 3 days), and a Super User group (14% of individuals) tracking 5

of every 7 days. If CDC would like to include longitudinal, ongoing data capture in the MCAM study, we would welcome the opportunity to partner on its use.

Response: Thank you for sharing your observations and your offer to collaborate on ongoing data capture. The app you described sounds like an excellent clinical tool for healthcare providers as well as an empowerment tool for the patients themselves. While we cannot implement the tool in the MCAM study given the ongoing nature of the research, we look forward to future discussions on tracking symptoms using an app.

Finally, we appreciate your time and thoughtful review, and for providing the Appendix table for data harmonization.