

NINDS CDE Project

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

Pain Subgroup

In drafting the recommendations and reviewing the current tools/instruments, the subgroup members reviewed the extant literature but also extracted information from the existing NINDS CDEs where some of the same tools are being used in other neurological conditions. Both the experiences of patients with ME/CFS and the experiences of clinicians who treat patients with ME/CFS were considered in the recommendations. One member of the subgroup is a person living with ME/CFS. Pediatric experts within the working group were asked to provide their recommendations for instruments and appropriate classifications.

Criteria for selection and classification:

- Relevance to ME/CFS pain symptoms presentation
- Validation of instrument with large national sample
- Relatively brief instrument but psychometrically sound and applicable to various populations
- Easy scoring system
- Accessible and free of charge

Functional limitations (e.g. length of surveys) were considered in the recommendations. While few instruments have been validated for ME/CFS, instruments that have been previously validated for similar conditions were also prioritized. Every attempt was made but due to the lack of validation for ME/CFS or ME/CFS-specific instruments, more work is needed to fully cover the diversity and complexity of ME/CFS clinical presentations. This heterogeneity may impact the performance and choice of an instrument or tool to assess a specific outcome.

Many symptoms of ME/CFS, including pain, are linked to post-exertional malaise (PEM), which means they wax and wane based on cognitive or physical effort. There is also a broad spectrum of the presence, type, nature and severity of pain across ME/CFS. Pain could be a minor aspect of illness, or the most disabling aspect of illness and presents across the entire pain spectrum (inflammatory, neuropathic, central sensitivity, etc).

In the literature, the research on fibromyalgia and the research on ME/CFS are separate. The overlap needs to be better understood. Every study should assess if patients meet the diagnosis for comorbid fibromyalgia and other chronic pain syndromes. There are two criteria used for fibromyalgia diagnosis, 1990 and 2010. There is not consensus as to which should be used. The 2010 criteria have overlap with ME/CFS criteria, particularly Fukuda. Questions have been added to the Pain Assessment CRF to collect information regarding whether or not fibromyalgia has been diagnosed and if so, which criteria were applied.

The Baseline/Covariate Subgroup is recommending either a combination of questions from the CDC Symptom Inventory and DePaul Symptom Questionnaire (DSQ) or the full DSQ as Core. These instruments query the presence, frequency and severity of pain but do not capture the significance or complexity of pain. The Pain Subgroup recommendations include tools to provide granularity.

As outlined in the IOM report 2015, pain is one of the least studied areas of ME/CFS, and the overlap with other pain conditions, especially fibromyalgia, has not been carefully explored in the literature. Assessment of pain in ME/CFS, done in a way that can be compared to other pain conditions, is an important area of need. Additional unmet needs include an instrument for measuring both pain and post-exertional malaise (PEM) together and as well as one designed to capture the multiple overlapping pain conditions that are associated with ME/CFS. A method for quantitatively assessing pain is also needed.

Recommendations Summary Table

Instrument/CRF Name	Population	Classification
Brief Pain Inventory (Short Form) (BPI)	Adult	Supplemental – Highly Recommended
Revised Fibromyalgia Impact Questionnaire (FIQR)	Adult	Supplemental – Highly Recommended
McGill Pain Questionnaire (MPQ)	Adult	Supplemental – Highly Recommended
Faces Pain Scale - Revised (FPS-R)	Pediatric	Supplemental – Highly Recommended
Pain Assessment	Adult; Pediatric	Supplemental (Supplemental-Highly Recommended: Pediatric Faces Pain Scale and Fibromyalgia Questions)
Pain Frequency-Severity-Duration Scale (PFSD)	Pediatric	Supplemental
Neuropathic Pain Symptom Inventory	Adult	Exploratory
PROMIS Pain Behavior Short Form	Adult	Exploratory
PROMIS Pain Interference Short Form	Adult	Exploratory