

Mitochondrial Disease Version 2.0 NINDS CDE Project Patient Reported Outcomes/Quality of Life/Fatigue Subgroup Summary

The NINDS Mitochondrial Disease v2.0 Common Data Element (CDE) Patient Reported Outcomes (PRO)/Quality of Life (QoL)/Fatigue Subgroup reviewed and updated CDEs based on advancements in neuroscientific clinical research. Patients with mitochondrial disease suffer from several multisystemic symptoms that can greatly impact their QoL, therefore, it was important for this group to assess a broad spectrum of PRO measures that include Health Related Quality of Life (HRQL) to allow for better evaluation of the impact of mitochondrial disease on day-to-day life and the effect of therapeutic interventions on patients. HRQL instruments assess physical, emotional and social impacts of the disease and may include objective functioning and subjective perceptions of health (Den Oudsten et al., 2007; Hunt, 1997).

The PRO/QoL/Fatigue Subgroup focused on instruments already reviewed in the CDE v1.0 project and added new instruments specifically focused on fatigue. PRO/QoL/Fatigue instruments are an integral part of mitochondrial disease assessments in both the clinical and research setting and have been extensively used in clinical trials. It is thus paramount to develop a well curated instrument database that may be useful for ongoing and future research in mitochondrial medicine.

The subgroup reassessed previously reviewed instruments and assessed new instruments for consideration. These instruments are primarily questionnaires to be either answered by patients and/or their caregivers or by the clinician/researcher evaluating the patient. Both adult and pediatric instruments were reviewed and included only a few mitochondrial disease validated measures.

The subgroup reviewed QoL and fatigue instruments which were recommended for inclusion in v2.0 while other instruments reviewed were unanimously excluded from the new version. Some of the instruments excluded have not been properly validated and have limited applicability to mitochondrial myopathy hence their exclusion.

For QoL instruments, the subgroup recommended the exclusion of the following from v2.0, the Craig Handicap and Assessment Reporting Technique (CHART - SF) Interview and Paper Versions, World Health Organization Quality of Life Assessment (WHOQOL-BREF) and Primary Mitochondrial Myopathy Symptom Assessment (PMMSA). The PMMSA was not recommended by this subgroup because it does not assess QoL. It is recommended by the General Medical/Neurological Assessments Subgroup because it includes disease manifestation and motor function which are within their purview.

While for fatigue scales, the subgroup excluded the following instruments from v2.0, Checklist for Individual Strength – Fatigue (CIS), Functional Assessment of Chronic Illness Therapy (FACIT) – Fatigue instruments, Multidimensional Fatigue Inventory (MFI), PROMIS Fatigue Short Form, PROMIS - 29 Profile, Mental Fatigue Scale (MFS) and Wood Mental Fatigue due to their inapplicability to mitochondrial disease.

Validated QoL CDEs are lacking. These CDEs are often dependent on age and on the overall health/cognitive status of a given participant. Due to these limitations, it was difficult to define universal CDEs for QoL within mitochondrial diseases

Overlap addressed with other subgroups includes evaluation of instruments pertaining to outcome measures for cognitive, behavioral, emotional and motor function. There are four instruments - the PedsQL, Fatigue Severity Scale (FSS), Quality of Life in Neurological Disorders (Neuro-QOL), and SF-36 - that overlap with the other subgroups.

The subgroup discussed including the PROMIS Fatigue Primary Mitochondrial Disease (PMD) Short Form as Supplemental – Highly Recommended, however, at the time the v2.0 CDEs were finalized, it was still pending publication. Addition of this instrument will be addressed in the future.

References

Den Oudsten BL, Van Heck GL, De Vries J. Quality of life and related concepts in Parkinson's disease: a systematic review. *Mov Disord.* 2007 Aug 15;22(11):1528-37.

Hunt SM. The problem of quality of life. *Qual Life Res.* 1997 Apr;6(3):205-12.

Summary of Recommendations

Subdomain	Instrument Name	Classification
Caregiver Reported Outcomes	Zarit Burden Interview (ZBI)	Supplemental – Highly Recommended
Fatigue	Fatigue Severity Scale (FSS)	Supplemental – Highly Recommended
	Modified Fatigue Impact Scale (MFIS)	Supplemental – Highly Recommended
	Pediatric Quality of Life Inventory, Multidimensional Fatigue Scale	Exploratory
NIH Resources	Quality of Life in Neurological Disorders (Neuro-QOL)/ Neuro-QOL Adult Bank – Fatigue	Supplemental – Highly Recommended
Quality of Life/Patient Reported Outcomes	12-Item Short Form Health Survey (SF-12)	Supplemental – Highly Recommended
	EuroQoL-5 Dimension Questionnaire (EQ-5D)	Supplemental – Highly Recommended
	Pediatric Quality of Life Inventory (PedsQL)	Supplemental – Highly Recommended
	Short Form 36-Item Health Survey (SF-36)	Supplemental – Highly Recommended