

Mitochondrial Disease CDE Highlight Summary Document

NIH Resources

The NINDS also strongly encourages researchers to use these NIH developed materials for NINDS-sponsored research, when appropriate. Utilization of these resources will enable greater consistency for NINDS-sponsored research studies. These tools are free of charge.

- National Institutes of Health (NIH) Toolbox
- Quality of Life in Neurological Disorders (Neuro-QOL)
- Patient-Reported Outcomes Measurement Information System (PROMIS)

Suicidal Ideation

Investigators should review the FDA's ["Guidance for Industry: Suicidal Ideation and Behavior: Prospective Assessment of Occurrence in Clinical Trials"](#) for the most up-to-date information about suicidal ideation and behavior. One scale that FDA suggests is the Columbia Suicide Severity Rating Scale (C-SSRS) (available at <https://cssrs.columbia.edu/>)

Disease/Domain; Subdomain	Recommendations and List of Forms
Mitochondrial Disease	<p>These instruments and elements are recommended for use in Mitochondrial Disease studies:</p> <p>Core Instruments: None</p> <p>Supplemental – Highly Recommended Instruments (for specific disease conditions or types of study): 12-Item Short Form Health Survey (SF-12); Apathy Evaluation Scale; Apathy Scale (AS); Automated Self-Administered 24-hour Dietary Recall (ASA 24); Barry Albright Dystonia Scale (BADs); Beck Anxiety Inventory (BAI); Beck Youth Inventories - 2nd Edition (BYI-II); Behavior Assessment System for Children, Third Edition (BASC-3); Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A); Behavior Rating Inventory of Executive Function - Second Edition (BRIEF-2); Behavior Rating Inventory of Executive Function- Preschool Version (BRIEF-P); Borg Rating of Perceived Exertion (RPE) Scale; Center for Epidemiologic Studies-Depression Scale (CES-D); Child Behavior Checklist (CBCL); Conners Continuous Performance Test 3rd Edition (Conners CPT 3); Delis-Kaplan Executive Function System (D-KEFS); EuroQoL-5 Dimension Questionnaire (EQ-5D); Fatigue Severity Scale (FSS); Generalized Anxiety Disorder (GAD-7); Mitochondrial Myopathy Composite Assessment Tool (MM-COAST); Modified Fatigue Impact Scale (MFIS); Modified Hammersmith Functional Motor Scale for Children with Spinal Muscular Atrophy (MHFMS-SMA/MHFMS-Extend); Motor Function Measure (MFM); Newcastle Mitochondrial Disease</p>

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	<p>Adult Scale (NMDAS); Newcastle Mitochondrial Quality of Life Measure (NMQ); Newcastle Paediatric Mitochondrial Disease Scale (NPMDS); Pediatric Quality of Life Inventory (PedsQL); Quality of Life in Neurological Disorders (Neuro-QOL); Scale for the Assessment and Rating of Ataxia (SARA); Short Form 36-Item Health Survey (SF-36); Test of Variables of Attention (TOVA); Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV); Zarit Burden Interview (ZBI)</p> <p>Core and Supplemental – Highly Recommended CDEs: See Start-Up Resource Listing document: Mitochondrial Disease Start-up Resource Listing</p>
NIH Resources/ NIH Resources	<p>Core: None</p> <p>Supplemental – Highly Recommended: Quality of Life in Neurological Disorders (Neuro-QOL)</p> <p>Supplemental: National Institutes of Health (NIH) Toolbox; Patient-Reported Outcomes Measurement Information System (PROMIS)</p> <p>Exploratory: None</p>
Participant Characteristics/ Demographics	<p>Core: General Core</p> <p>Supplemental – Highly Recommended: General Core</p> <p>Supplemental: None</p> <p>Exploratory: None</p>
Participant History and Family History/ General Health History	<p>Core: Family History; Medical History</p> <p>Supplemental – Highly Recommended: Diabetes-Related Medical History</p> <p>Supplemental: Bone Health History; Dietary Supplements; Family History; Medical History; Reproductive and Hormonal History</p> <p>Exploratory: Diabetes-Related Medical History</p>
Assessments and Examinations/ Audiology	<p>Core: Hearing Loss in Mitochondrial Disease</p> <p>Supplemental – Highly Recommended: Hearing Loss in Mitochondrial Disease; Vestibular Function in Mitochondrial Disease</p> <p>Supplemental: Vestibular Function in Mitochondrial Disease</p> <p>Exploratory: Hearing Loss in Mitochondrial Disease; Sensory Organization Test (SOT); Vestibular Function in Mitochondrial Disease</p>
Assessments and Examinations/ Exercise Physiology	<p>Core: None</p> <p>Supplemental – Highly Recommended: Staged Exercise Tolerance Test</p> <p>Supplemental: None</p> <p>Exploratory: None</p>

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Assessments and Examinations/ Imaging Diagnostics	<p>Core: Brain Magnetic Resonance Imaging (MRI); Head Computed Tomography (CT); Imaging - Mitochondrial Disease; Spine Magnetic Resonance Imaging (MRI)</p> <p>Supplemental – Highly Recommended: Brain Perfusion Magnetic Resonance Imaging (MRI); Echocardiogram; Magnetic Resonance Spectroscopy (MRS)</p> <p>Supplemental: Cardiac Magnetic Resonance Imaging (MRI); DXA</p> <p>Exploratory: Phosphorus Magnetic Resonance Spectroscopy (31P-MRS); Two Dimensional Speckle Tracking (Strain) Echocardiography Imaging</p>
Assessments and Examinations/ Laboratory Tests and Biospecimens/Biomarkers	<p>Core: Primary Mitochondrial Disease (PMD) Genetics</p> <p>Supplemental – Highly Recommended: Diabetes Labs; Primary Mitochondrial Disease (PMD) Genetics</p> <p>Supplemental: Biomarkers in Mitochondrial Disease; Diabetes Labs; Labs of Bone Mineral Metabolism; Primary Mitochondrial Disease (PMD) Genetics</p> <p>Exploratory: Diabetes Labs</p>
Assessments and Examinations/ Non-Imaging Diagnostics	<p>Core: None</p> <p>Supplemental – Highly Recommended: Electrocardiogram (ECG)</p> <p>Supplemental: Electrocardiogram (ECG); Holter Examination</p> <p>Exploratory: None</p>
Assessments and Examinations/ Physical Examinations	<p>Core: None</p> <p>Supplemental – Highly Recommended: Automated Self-Administered 24-hour Dietary Recall (ASA 24); Physical Exam</p> <p>Supplemental: Mitochondrial and Gastrointestinal Diseases Assessment</p> <p>Exploratory: None</p>
Assessments and Examinations/ Vital Signs and Other Body Measures	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Vital Signs</p> <p>Exploratory: None</p>
Outcomes and End Points/ Academic Achievement	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: American National Adult Reading Test (AMNART); Differential Ability Scales-II (DAS-II); Wechsler Individual Achievement Test-4 (WIAT-4)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Ataxia and Performance Measures	<p>Core: None</p> <p>Supplemental – Highly Recommended: Scale for the Assessment and Rating of Ataxia (SARA)</p> <p>Supplemental: International Cooperative Ataxia Rating Scale (ICARS)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Attention	<p>Core: None</p>

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	<p>Supplemental – Highly Recommended: Conners Continuous Performance Test 3rd Edition (Conners CPT 3); Test of Variables of Attention (TOVA)</p> <p>Supplemental: None</p> <p>Exploratory: None</p>
Outcomes and End Points/ Caregiver Reported Outcomes	<p>Core: None</p> <p>Supplemental – Highly Recommended: Zarit Burden Interview (ZBI)</p> <p>Supplemental: None</p> <p>Exploratory: None</p>
Outcomes and End Points/ Cognitive	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Automated Neuropsychological Assessment Metrics (ANAM); Brief Test of Adult Cognition by Telephone (BTACT); Cambridge Cognitive Examination-Revised (CAMCOG-R); Mini-Mental State Examination (MMSE); NEPSY-II; Repeatable Battery for Assessment of Neuropsychological Status (RBANS); Symbol Digit Modalities Test</p> <p>Exploratory: None</p>
Outcomes and End Points/ Dementia	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE); Montreal Cognitive Assessment (MoCA)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Digital Technology	<p>Core: None</p> <p>Supplemental – Highly Recommended: Exercise Wearables</p> <p>Supplemental: Exercise Wearables</p> <p>Exploratory: Exercise Wearables</p>
Outcomes and End Points/ Emotional/Behavioral	<p>Core: None</p> <p>Supplemental – Highly Recommended: Apathy Evaluation Scale; Apathy Scale (AS); Beck Anxiety Inventory (BAI); Beck Youth Inventories - 2nd Edition (BYI-II); Behavior Assessment System for Children, Third Edition (BASC-3); Center for Epidemiologic Studies-Depression Scale (CES-D); Child Behavior Checklist (CBCL); Generalized Anxiety Disorder (GAD-7)</p> <p>Supplemental: ALS Depression Inventory (ADI-12); Ask Suicide-Screening Questions (ASQ) Toolkit; Autism Diagnostic Interview - Revised (ADI-R); Autism Diagnostic Observation Schedule, Second Edition (ADOS-II); Brief Infant Toddler Social Emotional Assessment (BITSEA); Brief Psychiatric Rating Scale (BPRS); Cambridge Behavioral Inventory - Revised; Children's Depression Inventory - 2 (CDI-2); Columbia - Suicide Severity Rating Scale (C-SSRS); Hamilton Anxiety Rating Scale (HAM-A); Hamilton Depression Rating Scale (HDRS); Hospital Anxiety and</p>

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	Depression Scale (HADS); Irritability Scale (IS); Modified Overt Aggression Scale (MOAS); Montgomery-Asberg Depression Scale (MADRS); Mood Disorder Questionnaire (MDQ); Problem Behaviours Assessment HD - Short Version (PBA-s) Exploratory: None
Outcomes and End Points/ Executive Functioning	Core: None Supplemental – Highly Recommended: Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A); Behavior Rating Inventory of Executive Function - Second Edition (BRIEF-2); Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P); Delis-Kaplan Executive Function System (D-KEFS) Supplemental: Tower of London-Drexel University (TOLDX): 2nd Edition; Trail Making Test Exploratory: None
Outcomes and End Points/ Fatigue	Core: None Supplemental – Highly Recommended: Fatigue Severity Scale (FSS); Modified Fatigue Impact Scale (MFIS) Supplemental: None Exploratory: Pediatric Quality of Life Inventory, Multidimensional Fatigue Scale
Outcomes and End Points/ Intellectual Functioning	Core: None Supplemental – Highly Recommended: Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV) Supplemental: Kaufman Assessment Battery for Children; Leiter International Performance Scale-3 (Leiter-3); Reynolds Intellectual Assessment Scale, Second Edition (RIAS-2); Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II); Wechsler Adult Intelligence Scale - Fourth Edition (WAIS-IV); Wechsler Intelligence Scale for Children-V (WISC-V) Exploratory: None
Outcomes and End Points/ Language	Core: None Supplemental – Highly Recommended: None Supplemental: Boston Diagnostic Aphasia Exam (BDAA-3); Boston Naming Test (BNT) - 30-item version; Clinical Evaluation of Language Fundamentals - Fifth Edition (CELF-5); Comprehensive Assessment of Spoken Language, Second Edition (CASL-2); Controlled Oral Word Association Test (COWAT) Subtest of the Multilingual Aphasia Examination (MAE); Expressive One-Word Picture Vocabulary Test; New Reynell Developmental Language Scale (NRDLS); Peabody Picture Vocabulary Test 5th Edition (PPVT-5); Preschool Language Scales - Fifth Edition (PLS-5) Exploratory: None

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Outcomes and End Points/ Memory	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Brief Visuospatial Memory Test Revised (BVM-T-R); Child and Adolescent Memory Profile (ChAMP); Rey Auditory Verbal Learning Test (RAVLT); Rey Complex Figure Test and Recognition Trial (RCFT); Wechsler Memory Scale IV (WMS-IV); Wide Range Assessment of Memory and Learning, Third Edition (WRAML-3)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Motor Function	<p>Core: None</p> <p>Supplemental – Highly Recommended: Barry Albright Dystonia Scale (BADs); Borg Rating of Perceived Exertion (RPE) Scale; Mitochondrial Myopathy Composite Assessment Tool (MM-COAST); Modified Hammersmith Functional Motor Scale for Children with Spinal Muscular Atrophy (MHFMS-SMA/MHFMS-Extend); Motor Function Measure (MFM); Newcastle Mitochondrial Disease Adult Scale (NMDAS); Newcastle Paediatric Mitochondrial Disease Scale (NPMDS)</p> <p>Supplemental: 12 Minute Walking Test; 6 Minute Walk Test; Beery-Buktenica Developmental Test of Visual-Motor Integration (Beery VMI); Burke-Fahn-Marsden Movement Scale (BFMMS); Grooved Pegboard Test; Gross Motor Function Measure (GMFM-88, GMFM-66); International Pediatric Mitochondrial Disease Score (IPMDS); Peabody Developmental Motor Scale Second Edition (PDMS-2); Primary Mitochondrial Myopathy Symptom Assessment (PMMSA); Purdue Pegboard; Unified Dystonia Rating Scale (UDRS)</p> <p>Exploratory: 2 Minute Walk Test; Physical and Neurological Examination for Subtle Signs (PANESS)</p>
Outcomes and End Points/ Muscle Strength Testing	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Maximum Voluntary Isometric Contraction (MVIC)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Neuropsychological Testing	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Bayley Scales of Infant Development (Bayley III, BSID)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Pulmonary Function Testing/Respiratory Status	<p>Core: None</p> <p>Supplemental – Highly Recommended: Pulmonary Function</p> <p>Supplemental: Pulmonary Function</p> <p>Exploratory: None</p>

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Outcomes and End Points/ Quality of Life/Patient Reported Outcomes	<p>Core: None</p> <p>Supplemental – Highly Recommended: 12-Item Short Form Health Survey (SF-12); EuroQoL-5 Dimension Questionnaire (EQ-5D); Newcastle Mitochondrial Quality of Life Measure (NMQ); Pediatric Quality of Life Inventory (PedsQL); Short Form 36-Item Health Survey (SF-36)</p> <p>Supplemental: Child and Adolescent Scale of Environment (CASE); Child and Adolescent Scale of Participation (CASP)</p> <p>Exploratory: None</p>
Outcomes and End Points/ Sleep	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Epworth Sleepiness Scale (ESS) - Adult Version</p> <p>Exploratory: None</p>
Outcomes and End Points/ Visual-Spatial Processing	<p>Core: None</p> <p>Supplemental – Highly Recommended: None</p> <p>Supplemental: Judgment of Line Orientation (Benton JLO); Test of Visual Perceptual Skills - 4th Edition (TVPS-4)</p> <p>Exploratory: None</p>