

Mitochondrial Disease CDE Revision History Document

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March 2024 Revisions

Overview

The Mitochondrial Disease (Mito) Version 2.0 CDE Working Group comprehensively reviewed and updated the Mito Version 1.0 CDEs. There have been significant changes to the content of the Mito CDE materials in Version 2.0 compared to Version 1.0.

Updated or new Subgroup Summaries were posted for Mito Version 2.0 CDE Subgroups.

New Subdomains: Audiology and Exercise Physiology were added to the Assessments and Examinations Domain. Caregiver Reported Outcomes, Digital Technology, Fatigue, and Sleep were added to the Outcomes and End Points Domain.

The following guidance documents were updated or newly added to the Mito Version 2.0 recommendations.

Updated Guidance Documents (2)

1. Biomarkers Guidance Mitochondrial Disease F3141
 - a. Guidance was updated to include new references and content to match the revised Biomarkers in Mitochondrial Disease CRF.
2. Imaging Guidance and Definitions F3139
 - a. Guidance was updated to include addition of a table of normal myelination milestones, notes to the definitions for subependymal and central tegmental tract, and a new reference.

New Guidance Documents (1)

1. Mitochondrial Disease Ophthalmology Test Guidance F3140
 - a. This guidance document is a combination and update of the following v1.0 guidance documents: Mitochondrial Disease OCT Guidelines; Mitochondrial Disease Test Guidelines; Mitochondrial Disease Visual Electrophysiology Guidelines; Mitochondrial Disease Visual Fields Guidelines.

The following case report forms (CRFs) were updated, removed or newly added to the Mito Version 2.0 recommendations. The corresponding data dictionaries (i.e., CDE Detailed Reports) have been modified in accordance with the form changes. Notably, there were 228 CDEs added to the list of Core CDEs for all Mito studies from the Brain Magnetic Resonance Imaging (MRI); Family History; Head Computed Tomography (CT); Hearing Loss in Mitochondrial Disease; Imaging - Mitochondrial Disease; Medical History; Primary Mitochondrial Disease (PMD) Genetics; and Spine Magnetic Resonance Imaging (MRI) CRFs. There were no Core CDEs recommended in Mito v1.0. For the list of Core CDEs, see the Start-Up Resource Listing document: [Mitochondrial Disease Start-up Resource Listing](#).

Updated CRFs (15)

1. Biomarkers in Mitochondrial Disease F3091
 - a. CDEs Added
 - i. C02437 Imaging modality type
 - ii. C10682 Imaging anatomic site
 - iii. C18689 Imaging anatomic site other text
 - iv. C18701 Imaging modality type other text
 - v. C60224 Biomarker source assessment type other text
 - vi. C60225 Organoid type
 - vii. C60226 Organoid type other text
 - viii. C60227 Clinic assessment type
 - ix. C60228 Clinic assessment type other text
 - x. C60229 Cardiac evaluation type

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- xi. C60230 Cardiac evaluation type other text
- xii. C60231 EKG type
- xiii. C60232 Biomarker blood serum plasma assessment type other text
- xiv. C60233 Endocrine test type
- xv. C60234 Endocrine test type other text
- xvi. C60235 Hepatic panel type
- xvii. C60236 Hepatic panel type other text
- xviii. C60237 Metabolomic type
- xix. C60238 Vitamin level test type
- xx. C60239 Vitamin level test type other text
- xxi. C60240 Biomarker urine assessment type other text
- xxii. C60241 Biomarker cerebrospinal fluid assessment type other text
- xxiii. C60242 Biomarker fibroblast assessment type other text
- xxiv. C60243 Biomarker leukocyte assessment type other text
- xxv. C60244 Biomarker lymphoblast assessment type other text
- xxvi. C60245 Biomarker muscle biochemistry assessment type other text
- xxvii. C60246 Biomarker muscle histology assessment type other text
- xxviii. C60247 Biomarker genetic assessment type other text
- xxix. C60248 Biomarker specimen other source text
- b. CDEs Removed
 - i. C19552 Blood specimen lactate measurement status
 - ii. C19553 Blood specimen pyruvate measurement status
 - iii. C19554 Blood specimen lactate pyruvate ratio status
 - iv. C19559 Biomark neutrophils assessment type
 - v. C19560 Biomarker monocyte assessment type
 - vi. C19561 Biomarker platelet assessment type
 - vii. C19562 Biomarker lymphocyte assessment type
 - viii. C19568 Biomarker myotube assessment type
- c. Classification Changes
 - i. None
- d. Permissible Value Modifications
 - i. C19549 Biomarker source assessment type
 - 1. Added: Buccal swab; Cultured Cells; Imaging; Induced pluripotent stem cells (iPS); Kidney biopsy; Liver biopsy; Muscle biopsy; Organoid(s); Other, specify; Red blood cells; Saliva; Whole blood
 - 2. Removed: Genetic Testing; Liver biochemistry; Liver histology; Monocytes; Muscle biochemistry; Muscle histology; Myotubes; Neutrophils; Platelets (high OXPHOS)
 - 3. Revised: Blood to Blood (Serum/Plasma)
 - ii. C19551 Biomarker blood serum plasma assessment type
 - 1. Added: Acylcarnitines; CBC; Cell-free mitochondrial DNA (cf-mtDNA); Cystatin C; Electrolytes; Endocrine testing; Growth differentiation factor 15 (GDF15); LDH; Lipid panel; Other, specify; Purines and pyrimidines; Vitamin levels
 - 2. Removed: Deoxyuridine; fGSH/GSSG ratio; Free glutathione (fGSH); Leukocyte Coenzyme Q10; oxidized disulfide (GSSG); Plasma carbonyl content; Thymidine
 - 3. Revised: Amino acids (emphasis on alanine, alanine/lysine ratio, alanine/phenylalanine+lysine ratio, alanine/phenylalanine+lysine ratio, citrulline) to Amino acids; Hepatic enzymes (AST, ALT, GGT) to Hepatic panel; Metabolic profiling to Metabolomics
 - iii. C19555 Biomarker urine assessment type
 - 1. Added: Acylglycines; Metabolomics; mtDNA heteroplasmy; Other, specify; Purines and pyrimidines; Urinalysis (UA)
 - 2. Removed: 3-methylglutaconic acid; Lactate/creatinine

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- iv. C19556 Biomarker cerebrospinal fluid assessment type
 1. Added: 5-methyltetrahydrofolate; GABA; Metabolomics; Neurotransmitters; Other, specify; Protein
 2. Removed: CSF protein; lactate/pyruvate ratio
 3. Revised: Amino acids (emphasis on alanine, alanine/lysine ratio, alanine/phenylalanine+lysine ratio, alanine/phenylalanine+lysine ratio, citrulline) to Amino acids
- v. C19557 Biomarker fibroblast assessment type
 1. Added: Other, specify; Seahorse live cell metabolic analysis
 2. Removed: clear native gel OXPHOS enzymology; clear native gel OXPHOS immunoblot; Fibroblast OXPHOS subunit immunohistochemistry; OXPHOS subunit western blot; pyruvate dehydrogenase immunohistochemistry; pyruvate dehydrogenase subunit western blot
 3. Revised: Blue native gel electrophoresis to Blue native gel electrophoresis (OXPHOS)
- vi. C19558 Biomarker leukocyte assessment type
 1. Added: Intracellular free glutathione (fGSH), oxidized disulfide (GSSG), fGSH/GSSG ratio; Other, specify
 2. Removed: Intracellular coenzyme Q10; Intracellular free glutathione
- vii. C19563 Biomarker lymphoblast assessment type
 1. Added: Other, specify; Seahorse live cell metabolic analysis
- viii. C19564 Biomarker muscle biochemistry assessment type
 1. Added: ATP synthesis; Other, specify; Seahorse live cell metabolic analysis
 2. Removed: 8-oxoguanine DNA glycolase-1 (OCG-1); Aconitase enzymology; AIF; Bcl-2; Biogenesis regulator peroxisome proliferator-activated receptor-gamma coactivator- 1 alpha (PGC-1alpha); clear native gel OXPHOS enzymology; clear native gel OXPHOS immunoblot; Human mitochondrial transcription factor A (hmTFA or Tfam); Manganese superoxide dismutase (MnSOD); Mitochondrial DNA absence factor (midas); OXPHOS subunit western blot; pyruvate dehydrogenase subunit western blot
 3. Revised: Glutathione to Glutathione content
- ix. C19567 Biomarker muscle histology assessment type
 1. Added: Nicotinamide adenine dinucleotide tetrazolium reductase (NADH-TR); Other, specify
 2. Removed: Fibroblast growth factor 21 (fg21); Humanin immunochemistry; OXPHOS subunit immunochemistry
- x. C19569 Biomarker genetic assessment type
 1. Added: Gene sequencing panel; Other, specify; RNA analysis; Whole genome sequencing
 2. Removed: Cellular energetics gene sequencing (NGS) (nDNA +mtDNA)
 3. Revised: mtDNA copy number (Leukocytes) and mtDNA copy number (muscle) to mtDNA copy number; mtDNA deletion/duplication (Leukocytes) and mtDNA deletion/duplication (muscle) to mtDNA deletion/duplication
- 2. Brain Magnetic Resonance Imaging (MRI) F3136
 - a. CDEs Added
 - i. C13977 Imaging abnormality cortical anatomic site
 - ii. C18027 Comment text
 - iii. C22866 Imaging magnetic resonance imaging date and time
 - iv. C60059 Imaging brain magnetic resonance imaging perform greater than six count
 - v. C60060 Imaging radio frequency coil channel count text
 - vi. C60061 Imaging contrast agent dose unit of measure
 - vii. C60062 Imaging diffusion-weighted imaging sequence type
 - viii. C60063 Imaging diffusion b-value type
 - ix. C60064 Imaging diffusion b-value type other text
 - x. C60065 Imaging quality technically satisfactory partial specify text
 - xi. C60066 Imaging cortical migration anomaly indicator
 - xii. C60067 Imaging cortical migration anomaly anatomic site

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- xiii. C60068 Imaging commissural fiber normality status
 - xiv. C60069 Imaging striatum normality status
 - xv. C60070 Imaging T2 weighted white matter abnormality pattern type
 - xvi. C60071 Imaging anterior limb internal capsule change status
 - xvii. C60072 Imaging posterior limb internal capsule change status
 - xviii. C60073 Imaging diffusion-weighted imaging white matter normality status
 - xix. C60074 Imaging diffusion-weighted imaging white matter abnormality anatomic site
 - xx. C60075 Imaging diffusion-weighted imaging white matter abnormality characteristic specify text
 - xxi. C60076 Imaging cavitation indicator
 - xxii. C60077 Imaging cavitation anatomic site
 - xxiii. C60078 Imaging cortical involve type
 - xxiv. C60079 Imaging cortical involve type other text
 - xxv. C60080 Imaging subependymal cyst indicator
 - xxvi. C60081 Imaging subependymal cyst anatomic site
 - xxvii. C60082 Imaging brain abnormal enhancement indicator
 - xxviii. C60083 Imaging brain abnormal enhancement anatomic site
- b. CDEs Removed
- i. C08254 Imaging visual analysis location performed type
 - ii. C10568 Imaging radio frequency coil channel count
 - iii. C10682 Imaging anatomic site
 - iv. C12476 Imaging other incidental finding indicator
 - v. C12477 Imaging other incidental finding type
 - vi. C12478 Imaging cortex-pachygyria indicator
 - vii. C12479 Imaging cortex-pachygyria site type
 - viii. C12480 Imaging cortex-pachygyria thickness measurement
 - ix. C12481 Imaging cortex lissencephaly (LIS type 1) indicator
 - x. C12482 Imaging cortex lissencephaly (LIS type 1) thickness measurement
 - xi. C12483 Imaging cortex-polymicrogyria indicator
 - xii. C12484 Imaging cortex-polymicrogyria site type
 - xiii. C12485 Imaging other cortical abnormality indicator
 - xiv. C12486 Imaging other cortical abnormality type
 - xv. C12487 Imaging other cortical abnormality site type
 - xvi. C12488 Imaging subcortical cyst indicator
 - xvii. C12489 Imaging subcortical cysts site type
 - xviii. C12493 Imaging brainstem abnormality type
 - xix. C12494 Imaging pons abnormal indicator
 - xx. C12495 Imaging pons abnormality type
 - xxi. C12497 Imaging cerebellum abnormality type
 - xxii. C12501 Imaging internal capsule type indicator
 - xxiii. C17931 Imaging magnetic resonance imaging performed indicator
 - xxiv. C18610 Imaging in plane resolution axis 2 measurement
 - xxv. C18611 Imaging field of view axis 2 measurement
 - xxvi. C18689 Imaging anatomic site other text
 - xxvii. C18714 Imaging radio frequency coil channel count other text
 - xxviii. C18715 Imaging radio frequency coil other text
 - xxix. C18719 Imaging slice orientation type other text
 - xxx. C18720 Imaging visual analysis location performed type other text
 - xxxi. C18854 Imaging other incidental finding other text
 - xxxii. C18855 Imaging other cortical abnormality other text
 - xxxiii. C18857 Imaging brainstem abnormality other text

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- xxxiv. C18858 Imaging pons abnormality other text
- xxxv. C18859 Imaging cerebellum abnormality other text
- c. Classification Changes
 - All CDEs: Supplemental (v1.0) to Core (v2.0)
 - i. C00008 Age value
 - ii. C01520 Head circumference measurement
 - iii. C02495 Imaging scanner strength value type
 - iv. C02496 Imaging scanner manufacturer name
 - v. C02499 Imaging pulse sequence type
 - vi. C08023 Imaging abnormal finding text
 - vii. C08238 Imaging repetition gap duration
 - viii. C08239 Imaging echo duration
 - ix. C08241 Imaging field of view axis 1 measurement
 - x. C08242 Imaging acquisition duration
 - xi. C08244 Imaging slice thickness value
 - xii. C08245 Imaging slice count
 - xiii. C08255 Imaging visual analysis blinded indicator
 - xiv. C10567 Imaging radio frequency coil type
 - xv. C10570 Imaging contrast agent used indicator
 - xvi. C10576 Imaging in plane resolution axis 1 measurement
 - xvii. C10685 Imaging slice orientation type
 - xviii. C10837 Imaging gap between slices measurement
 - xix. C10927 Imaging inversion time duration
 - xx. C10931 Imaging quality technically satisfactory status
 - xxi. C10932 Imaging lesion found indicator
 - xxii. C10933 Imaging lesion found type
 - xxiii. C12467 Imaging brain magnetic resonance imaging perform multiple status
 - xxiv. C12468 Imaging magnetic resonance imaging performed multiple count type
 - xxv. C12469 Imaging magnetic resonance imaging session number
 - xxvi. C12474 Imaging field of view measurement description text
 - xxvii. C12475 Imaging magnetic resonance imaging T1 T2 sequence name
 - xxviii. C12490 Imaging ventricle normality status
 - xxix. C12491 Imaging ventricle abnormality type
 - xxx. C12492 Imaging brainstem normality status
 - xxxi. C12496 Imaging cerebellum normality status
 - xxxii. C12498 Imaging T2 white matter status
 - xxxiii. C12499 Imaging T2 weighted white matter abnormality site type
 - xxxiv. C12500 Imaging corpus callosum change status
 - xxxv. C12502 Imaging anterior commissure change status
 - xxxvi. C12503 Imaging T2 fluid attenuated inversion recovery gray matter hyperintensity indicator
 - xxxvii. C12504 Imaging T2 fluid attenuated inversion recovery gray matter hyperintensity anatomic site
 - xxxviii. C12505 Imaging eye abnormality indicator
 - xxxix. C12506 Imaging eye abnormality type
 - xl. C14964 Sedation used indicator
 - xli. C17402 Site name
 - xl. C17798 Imaging contrast agent name
 - xl. C17925 Imaging contrast agent dose
 - xl. C18708 Imaging pulse sequence type other text
 - xl. C18716 Imaging scanner manufacturer name other text
 - xl. C18718 Imaging scanner strength value type other text

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- xlvi. C18813 Imaging lesion found other text
- xlviii. C18856 Imaging ventricle abnormality other text
- xlx. C18860 Imaging T2 fluid attenuated inversion recovery gray matter hyperintensity anatomic site other text
- d. Permissible Value Modifications
 - i. C02495 Imaging scanner strength value type
 - 1. Removed: 4.0T
 - ii. C02499 Imaging pulse sequence type
 - 1. Added: DWI; GE; SWI
 - iii. C10931 Imaging quality technically satisfactory status
 - 1. Added: Partially, specify
 - iv. C10933 Imaging lesion found type
 - 1. Added: Brainstem; Cerebellum; Cortical; Globus Pallidus; Striatal; Thalamic; WM
 - 2. Removed: Grey matter hyperintensity; Infarct; Malformation; WM hyperintensity
 - v. C12499 Imaging T2 weighted white matter abnormality site type
 - 1. Added: Brainstem; Superficial
 - 2. Removed: Diffuse
 - 3. Revised: Cerebellar WM to Cerebellar; Deep WM to Deep
 - vi. C12504 Imaging T2 fluid attenuated inversion recovery gray matter hyperintensity anatomic site
 - 1. Added: Cortex
- 3. Brain Perfusion Magnetic Resonance Imaging (MRI) F3088
 - a. CDEs Added
 - i. C08240 Imaging flip angle measurement
 - ii. C10578 Imaging label pulse duration
 - iii. C10839 Imaging volume count
 - iv. C15580 Imaging acquisition type
 - v. C19019 Imaging acquisition type other text
 - vi. C20247 Imaging scanner model name text
 - vii. C60061 Imaging contrast agent dose unit of measure
 - viii. C60084 Imaging preload contrast agent previous injection indicator
 - ix. C60085 Imaging preload contrast agent previous injection dose value
 - x. C60086 Imaging post processing analysis type
 - xi. C60087 Imaging post processing analysis method software provided type
 - xii. C60088 Imaging post processing analysis method software provided type other text
 - xiii. C60089 Imaging post processing analysis method software leakage correction indicator
 - xiv. C60090 Parameter map calculation other text
 - xv. C60091 Imaging arterial spin labeling scheme type
 - xvi. C60092 Imaging arterial spin labeling scheme type other text
 - xvii. C60093 Imaging arterial spin labeling acquisition type
 - xviii. C60094 Imaging arterial spin labeling phase type
 - xix. C60095 Imaging arterial spin labeling single phase type delay time
 - xx. C60096 Imaging arterial spin labeling multiphase type phase count
 - xxi. C60097 Imaging post processing analysis method quantitative indicator
 - xxii. C60098 Imaging crusher gradient use indicator
 - b. CDEs Removed
 - i. C08236 Imaging scanner software name
 - ii. C08241 Imaging field of view axis 1 measurement
 - iii. C08242 Imaging acquisition duration
 - iv. C08244 Imaging slice thickness value
 - v. C08245 Imaging slice count
 - vi. C10567 Imaging radio frequency coil type

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- vii. C10568 Imaging radio frequency coil channel count
- viii. C10570 Imaging contrast agent used indicator
- ix. C10576 Imaging in plane resolution axis 1 measurement
- x. C10577 Imaging signal averages number
- xi. C10583 Imaging base resolution value
- xii. C10584 Imaging phase resolution percentage value
- xiii. C10585 Imaging phase partial Fourier indicator
- xiv. C10586 Imaging bandwidth value
- xv. C10587 Imaging echo spacing value
- xvi. C10588 Imaging echo train length measurement
- xvii. C10589 Imaging shot count
- xviii. C10590 Imaging interpolation indicator
- xix. C10591 Imaging phase encode direction text
- xx. C10592 Imaging flow compensation indicator
- xxi. C10593 Imaging fat signal suppressed indicator
- xxii. C10594 Imaging parallel acquisition used indicator
- xxiii. C10595 Imaging parallel acquisition used type
- xxiv. C10842 Imaging analysis software name
- xxv. C10843 Imaging analysis software version number
- xxvi. C18690 Imaging analysis software other text
- xxvii. C18703 Imaging parallel acquisition used other text
- xxviii. C18715 Imaging radio frequency coil other text
- xxix. C58646 Imaging phase partial Fourier ratio text
- c. Classification Changes
 - All CDEs: Supplemental (v1.0) to Supplemental – Highly Recommended (v2.0)
 - i. C02495 Imaging scanner strength value type
 - ii. C02496 Imaging scanner manufacturer name
 - iii. C02498 Imaging scanner software version number text
 - iv. C02499 Imaging pulse sequence type
 - v. C08238 Imaging repetition gap duration
 - vi. C08239 Imaging echo duration
 - vii. C10569 Imaging perfusion method type
 - viii. C10599 Parameter map calculation type
 - ix. C17797 Imaging contrast agent injection rate
 - x. C17798 Imaging contrast agent name
 - xi. C17925 Imaging contrast agent dose
 - xii. C18708 Imaging pulse sequence type other text
 - xiii. C18716 Imaging scanner manufacturer name other text
 - xiv. C18718 Imaging scanner strength value type other text
- d. Permissible Value Modifications
 - i. C02495 Imaging scanner strength value type
 - 1. Removed: 4.0T
 - ii. C02496 Imaging scanner manufacturer name
 - 1. Added: Canon
 - 2. Removed: Agfa; Carestream; Hitachi; Hologic; Konica Minolta; Toshiba
 - iii. C02499 Imaging pulse sequence type
 - 1. Removed: CE MRA; Continuous-ASL; COW MRA; DIR; DTI; Dual echo PD/T2W SE; DWI; DWI/ADC; EPI; FLAIR; FLASH; fMRI; GRE; ISIS; MPRAGE; MRSI; Multivoxel spectroscopy; PD SE; PD/T2W FSE; Post-contrast FLAIR; Post-contrast T1-weighted; PRESS; Pseudocontinuous-ASL; PSIR; Pulsed-ASL; PWI; rFOV; Single voxel spectroscopy (SVS); SPACE/VISTA; Spectroscopic imaging 2D; Spectroscopic

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imaging 3D; SPGR; STEAM; SWI; T1; T1W 3D gradient-echo; T1W SE; T1-weighted spin echo with contrast; T1-weighted spin echo without contrast; T2; T2W SE; TOF Neck MRA; TSE/FSE; Unlocalized spectroscopy

- iv. C10599 Parameter map calculation type
 - 1. Added: Blood arrival time or similar; Cerebral blood flow; Other, specify; Time to maximum seconds
- 4. Cardiac Magnetic Resonance Imaging (MRI) F1056
 - a. CDEs Added
 - i. C02411 Laterality type
 - b. CDEs Removed
 - i. None
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C12857 Cardiac MRI myocardial scar segment anatomic site
 - 1. Added: 1 - Normal; 2 - Hypokinetic; 3 - Akinetic; 4 - Dyskinetic; 5 - Aneurysmal; X - Cannot Interpret
- 5. Diabetes Labs F3092
 - a. CDEs Added
 - i. C01711 Lab test result unit of measure
 - ii. C57974 Laboratory procedure random glucose measurement
 - iii. C60249 Laboratory procedure anti-pancreatic autoantibody name
 - b. CDEs Removed
 - i. None
 - c. Classification Changes
 - i. C19725 Laboratory procedure two hour glucose measurement: Supplemental – Highly Recommended (v1.0) to Supplemental (v2.0)
 - d. Permissible Value Modifications
 - i. None
- 6. Diabetes-Related Medical History F3085
 - a. CDEs Added
 - i. C06358 Diabetes mellitus type
 - ii. C19722 Laboratory procedure glycosylated hemoglobin measurement
 - iii. C20003 Hypoglycemia diagnosis indicator
 - iv. C20004 Hypoglycemia diagnosis type
 - v. C20005 Hypoglycemia symptom diagnosis text
 - vi. C20269 Insulin delivery method last use type
 - vii. C58756 Lab test result standard unit of measure
 - viii. C59704 Hyperglycemia history indicator
 - ix. C59705 Pre-diabetes diagnosis ever indicator
 - x. C59707 Hypoglycemia history indicator
 - xi. C59713 Hospitalization diabetes diagnosis indicator
 - xii. C59743 Genetic test diabetes indicator
 - xiii. C59744 Genetic test diabetes result text
 - xiv. C59745 BMI diabetes diagnosis category
 - xv. C59746 Glycosylated hemoglobin diabetes diagnosis value
 - xvi. C59747 Glycosylated hemoglobin measure method type
 - xvii. C59748 Participant mother pregnancy diabetes status
 - xviii. C59749 Family history insulin current use indicator
 - xix. C59750 Blood glucose test method type
 - xx. C59751 Insulin basal current use status
 - xxi. C59752 Insulin bolus current use status

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- xxii. C59753 Insulin neutral protamine hagedorn dose
 - xxiii. C59754 Insulin premix dose
 - xxiv. C59755 Insulin inject difficult status
 - xxv. C59756 Insulin inject difficult type
 - xxvi. C59757 Insulin inject difficult type other text
 - xxvii. C59758 Medication diabetes not insulin current former indicator
 - xxviii. C59759 Medication diabetes biguanide status
 - xxix. C59760 Medication diabetes sulfonylurea status
 - xxx. C59761 Medication diabetes thiazolidinedione status
 - xxxi. C59762 Medication diabetes GLP-1 agonist status
 - xxxii. C59763 Medication diabetes DPP-4 inhibitor status
 - xxxiii. C59764 Medication diabetes SGLT2 inhibitor status
 - xxxiv. C59765 Medication diabetes other not insulin status
 - xxxv. C59766 Medication diabetes combination status
 - xxxvi. C59767 Medical office visit diabetes past year count unknown status
 - xxxvii. C59768 Medical office visit not diabetes related past year count unknown status
 - xxxviii. C59769 Dietician consult count unknown status
 - xxxix. C59770 Medication hypoglycemia indicator
 - xl. C59771 Medication hypoglycemia type
 - xli. C59772 Hypoglycemia feed change indicator
 - xl. C59773 Hypoglycemia feed change type
 - xl. C59774 Hypoglycemia cause indicator
 - xl. C59775 Hypoglycemia diagnosis reason
 - b. CDEs Removed
 - i. C00709 Tobacco cigarettes smoked daily average number
 - ii. C16160 Tobacco smoked 100 cigarettes indicator
 - iii. C18153 Data unknown text
 - iv. C20256 Physical activity 20 minute day during week count
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C19670 Family history diagnosis age unknown status; C20277 Emergency room use past year indicator; C20283 911 call diabetes past year indicator; C20289 Urgent care clinic use past year indicator; C20295 Hospital admission past year indicator; C20301 Medical office visit past year indicator; C20308 Dietician consult past year indicator
 - 1. Revised: Don't know to Unknown
 - ii. C18241 Diagnosis age value unit of measure
 - 1. Added: Years (21 years and older)
 - iii. C20242 Diabetes clinical symptom presentation diagnosis type
 - 1. Added: Fatigue
 - 2. Removed: Diabetic ketoacidosis
 - iv. C20243 Diabetes laboratory diagnosis type
 - 1. Added: Diabetic ketoacidosis
 - v. C20258 Medication reduce blood sugar prior diagnosis type
 - 1. Added: GLP1RA; SGLT2i
7. Dietary Supplements F3086
- a. CDEs Added
 - i. C59695 Dietary supplement study use day count
 - ii. C59696 Dietary supplement multivitamin or mineral name
 - iii. C59697 Dietary supplement individual name

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- iv. C59698 Dietary supplement dose unit of measure
 - v. C59699 Dietary supplement route type other text
 - b. CDEs Removed
 - i. None
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C19715 Dietary supplement generic name
 - 1. Added: Beta Carotene; Bicarbonate; Brewer's yeast; Choline; Chromium; Cod liver oil; Coenzyme Q10 as ubiquinol; Coenzyme Q10 as ubiquinone; Creatine; DHEA; Dichloroacetate; Echinacea; Evening primrose; Fiber; Flax Seed Oil; Flaxseed; Ginkgo; Ginseng; Glucosamine/Chondroitin; Idebenone; Lecithin; Lycopene; Melatonin; Methylfolate; Nicotinamide riboside; Omega-3 fatty acids; Polyphenols; Pyrroloquinoline quinone (PQQ); Saw Palmetto; Soy Protein Powder; Soy Supplements; St. John's Wort; Turmeric; Vitamin B12 (cobalamin); Vitamin E (tocopherol); Vitamin K (phyloquinone); Weight Loss Supplements; Wheat Germ; Zinc
 - 2. Removed: Coenzyme Q10; Creatinine
 - 3. Revised: Carnitine to L-Carnitine; Lipoic acid (thiotic acid) to Alpha-lipoic acid (thiotic acid)
8. Echocardiogram F3137
- a. CDEs Added
 - i. None
 - b. CDEs Removed
 - i. C18878 Echocardiogram result other text
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. None
9. Holter Examination F1059
- a. CDEs Added
 - i. C59694 Tachycardia episode unit of measure
 - b. CDEs Removed
 - i. C12921 Cardiovascular Holter exam episode count type
 - ii. C18881 Cardiovascular Holter exam episode count other text
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. None
10. Imaging - Mitochondrial Disease F3089
- a. CDEs Added
 - i. C60169 Imaging development malformation miscellaneous anatomic site
 - b. CDEs Removed
 - i. None
 - c. Classification Changes
 - All CDEs: Supplemental (v1.0) to Core (v2.0)
 - i. C02411 Laterality type
 - ii. C19687 Imaging cerebrum component type
 - iii. C19688 Imaging cerebrum finding type
 - iv. C19689 Imaging cerebrum lobe anatomic site
 - v. C19690 Imaging white matter anatomic site
 - vi. C19691 Imaging deep grey nuclei anatomic site
 - vii. C19692 Imaging cerebellum finding type

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- viii. C19693 Imaging brainstem finding type
- ix. C19694 Imaging development malformation corpus callosum type
- x. C19695 Imaging development malformation cerebellum type
- xi. C19696 Imaging development malformation polymicrogyria anatomic site
- xii. C19697 Imaging development malformation heterotopia anatomic site
- xiii. C19698 Imaging myelination type
- xiv. C19699 Imaging myelination abnormal distribution text
- xv. C19700 Imaging myelination pattern calculated age value
- xvi. C19703 Imaging cerebellum component type
- xvii. C19997 Imaging deep grey nuclei finding type
- xviii. C19998 Imaging white matter tract finding type
- xix. C19999 Imaging white matter tract type

d. Permissible Value Modifications

- i. None

11. Mitochondrial and Gastrointestinal Diseases Assessment F3093

a. CDEs Added

- i. C60271 Mitochondrial disease DNA deletion text
- ii. C60272 Informant questionnaire text
- iii. C60273 Mitochondrial disease infant formula choose reason text
- iv. C60274 Mitochondrial disease infant formula recommendation type
- v. C60275 Mitochondrial disease infant formula recommendation type other text
- vi. C60276 Mitochondrial disease prior special diet type
- vii. C60277 Mitochondrial disease stop diet reason text
- viii. C60278 Mitochondrial disease prior special diet affect symptom text
- ix. C60279 Mitochondrial disease vomit characteristic type
- x. C60280 Mitochondrial disease prior vomit fail stop text
- xi. C60281 Mitochondrial disease abdominal migraine diagnosis indicator
- xii. C60282 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn frequency type other text
- xiii. C60283 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn meal timing interval
- xiv. C60284 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn trigger text
- xv. C60285 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn relief text
- xvi. C60286 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn season variation text
- xvii. C60287 Mitochondrial disease prior GERD heartburn mid-line chest pain esophageal burn frequency type other text
- xviii. C60288 Mitochondrial disease swallow difficult indicator
- xix. C60289 Mitochondrial disease swallow difficult onset age category
- xx. C60290 Mitochondrial disease swallow difficult occur liquid solid type
- xxi. C60291 Mitochondrial disease swallow difficult frequency type
- xxii. C60292 Mitochondrial disease swallow difficult frequency type other text
- xxiii. C60293 Mitochondrial disease swallow pain indicator
- xxiv. C60294 Mitochondrial disease swallow pain onset age category
- xxv. C60295 Mitochondrial disease swallow pain occur liquid solid type
- xxvi. C60296 Mitochondrial disease swallow pain frequency type other text
- xxvii. C60297 Mitochondrial disease swallow pain consistent indicator
- xxviii. C60298 Mitochondrial disease swallow pain change status
- xxix. C60299 Mitochondrial disease good appetite indicator
- xxx. C60300 Mitochondrial disease recent change appetite indicator

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- xxxi. C60301 Mitochondrial disease early satiety indicator
- xxxii. C60302 Mitochondrial disease choke liquid indicator
- xxxiii. C60303 Mitochondrial disease choke solid indicator
- xxxiv. C60304 Mitochondrial disease swallow position change indicator
- xxxv. C60305 Mitochondrial disease cough eat indicator
- xxxvi. C60306 Mitochondrial disease tired eat indicator
- xxxvii. C60307 Mitochondrial disease distract eat indicator
- xxxviii. C60308 Mitochondrial disease difficult breath eat indicator
- xxxix. C60309 Mitochondrial disease drool indicator
 - xl. C60310 Mitochondrial disease voice change eating indicator
 - xli. C60311 Mitochondrial disease dysphagia diagnosis type
 - xl.ii. C60312 Mitochondrial disease swallow study indicator
 - xl.iii. C60313 Mitochondrial disease swallow study result type
 - xl.iv. C60314 Mitochondrial disease swallow center feed therapist indicator
 - xl.v. C60315 Mitochondrial disease swallow center feed therapist recommendation type
 - xl.vi. C60316 Mitochondrial disease fiberoptic endoscopic evaluation of swallowing indicator
 - xl.vii. C60317 Mitochondrial disease current abdominal pain trigger type other text
 - xl.viii. C60318 Mitochondrial disease prior abdominal pain reason other text
 - xl.ix. C60319 Mitochondrial disease prior abdominal pain trigger type other text
 - I. C60320 Mitochondrial disease bowel movements current medication type other text
 - li. C60321 Mitochondrial disease pancreatic diagnose indicator
 - lii. C60322 Mitochondrial disease pancreatitis episode type
 - liii. C60323 Mitochondrial disease pancreatitis episodes occur text
 - liv. C60324 Mitochondrial disease pancreatitis episodes duration text
 - lv. C60325 Mitochondrial disease first pancreatitis episode age value
 - lvi. C60326 Mitochondrial disease last pancreatitis episode age value
 - lvii. C60327 Mitochondrial disease total pancreatitis episodes number
 - lviii. C60328 Mitochondrial disease acute pancreatitis indicator
 - lix. C60329 Mitochondrial disease recurrent acute pancreatitis indicator
 - lx. C60330 Mitochondrial disease chronic pancreatitis indicator
 - lxi. C60331 Mitochondrial disease pancreas insufficiency indicator
 - lxii. C60332 Mitochondrial disease symptom prompt check pancreatitis text
 - lxiii. C60333 Mitochondrial disease pancreatitis hospitalize indicator
 - lxiv. C60334 Mitochondrial disease pancreas imaging study indicator
 - lxv. C60335 Mitochondrial disease pancreas imaging study type
 - lxvi. C60336 Mitochondrial disease genetic testing pancreas indicator
 - lxvii. C60337 Mitochondrial disease genetic tests pancreas result text
 - lxviii. C60338 Mitochondrial disease fecal elastase test indicator
 - lxix. C60339 Mitochondrial disease fecal elastase test result status
 - lxx. C60340 Mitochondrial disease pancreatic enzyme replacement therapy indicator
 - lxxi. C60341 Mitochondrial disease chronic pain medication pancreatitis indicator
- b. CDEs Removed
 - i. C01581 Weight unit of measure
 - ii. C01582 Height unit of measure
 - iii. C20040 Mitochondrial disease eat reason text
 - iv. C20100 Mitochondrial disease GI detail text
 - v. C20139 Mitochondrial disease swallow difficult pain type
 - vi. C20140 Mitochondrial disease swallow problem onset age category
 - vii. C20141 Mitochondrial disease swallow problem occur liquid solid type
 - viii. C20142 Mitochondrial disease swallow problem frequency

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- ix. C20153 Mitochondrial disease feed difficult text
- x. C20210 Mitochondrial disease defecation other treatment text
- c. Classification Changes
 - i. None
- d. Permissible Value Modifications
 - i. C20049 Mitochondrial disease current vomit onset age category; C20069 Mitochondrial disease prior vomit onset age category; C20070 Mitochondrial disease prior vomit stop age category; C20095 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn onset age category; C20101 Mitochondrial disease prior GERD heartburn mid-line chest pain esophageal burn onset age category; C20102 Mitochondrial disease prior GERD heartburn mid-line chest pain esophageal burn stop age category; C20110 Mitochondrial disease current oral regurgitation onset age category; C20116 Mitochondrial disease prior oral regurgitation onset age category; C20117 Mitochondrial disease prior oral regurgitation stop age category; C20125 Mitochondrial disease current burp onset age category; C20131 Mitochondrial disease prior burp onset age category; C20132 Mitochondrial disease prior burp stop age category; C20154 Mitochondrial disease current abdominal pain onset age category; C20170 Mitochondrial disease prior abdominal pain onset age category; C20171 Mitochondrial disease prior abdominal pain stop age category; C20189 Mitochondrial disease current bloat abdominal distension onset age category; C20194 Mitochondrial disease prior bloat abdominal distension onset age category; C20195 Mitochondrial disease prior bloat abdominal distension stop age category; C20204 Mitochondrial disease bowel movement problem onset age category
 - 1. Revised: Age range permissible values were updated to address gaps
 - a. [2 mo to 5 mo] to [2 mo through 5.9 mo]
 - b. [6 mo to 12 mo] to [6 mo through 12.9 mo]
 - c. [13 mo to 18 mo] to [13 mo through 18.9 mo]
 - d. [19 mo to 3 y] to [19 mo through 3.9 y]
 - e. [4 y to 6 y] to [4 y through 6.9 y]
 - f. [7 y to 13 y] to [7 y through 13.9 y]
 - g. [14 y to 18 y] to [14 y through 18.9 y]
 - ii. C20053 Mitochondrial disease current vomit frequency type; C20073 Mitochondrial disease prior vomit frequency type; C20087 Mitochondrial disease prior vomit onset trigger type; C20097 Mitochondrial disease current GERD heartburn mid-line chest pain esophageal burn frequency type; C20105 Mitochondrial disease prior GERD heartburn mid-line chest pain esophageal burn frequency type; C20112 Mitochondrial disease current oral regurgitation frequency type; C20120 Mitochondrial disease prior oral regurgitation frequency type; C20145 Mitochondrial disease swallow pain frequency type; C20159 Mitochondrial disease current abdominal pain frequency type; C20163 Mitochondrial disease current abdominal pain trigger type; C20176 Mitochondrial disease prior abdominal pain frequency type; C20180 Mitochondrial disease prior abdominal pain trigger type; C20237 Mitochondrial disease Munchausen by proxy syndrome health care professional setting type
 - 1. Revised: Other to Other, specify
 - iii. C20034 Mitochondrial disease person relationship category
 - 1. Revised: Guardian to Guardian (not a relative); Other to Other, specify
 - iv. C20037 Mitochondrial disease problem type
 - 1. Added: Blood in the stool; Constipation; Diarrhea; Fecal incontinence; Nausea; Pain with bowel movements; Post-prandial distress; Straining
 - 2. Removed: Problems with bowel movements
 - 3. Revised: Difficulty or pain with swallowing to Difficulty swallowing and Pain with swallowing
 - v. C20038 Mitochondrial disease eat type
 - 1. Revised: Eats by himself to Eats by oneself
 - vi. C20043 Mitochondrial disease current special diet type
 - 1. Added: Enteral feed

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2. Revised: Fructose to Fructose free; Low fermentable oligo-Di-Monosaccharides and Polyols to Low fermentable oligo-Di-Monosaccharides and Polyols (Low FODMAP); Other to Other, specify
 - vii. C20048 Mitochondrial disease vomit current prior status
 1. Added: Never
 - viii. C20050 Mitochondrial disease current vomit episode trigger symptom onset type
 1. Added: History of recent COVID-19 infection
 2. Revised: Other to Other specify
 - ix. C20059 Mitochondrial disease current vomit before problem type
 1. Revised: Right after feeding to Right after or within 30 minutes of feeding
 - x. C20146 Mitochondrial disease swallow pain disrupt activity wake type
 1. Revised: Pain wakes child and disrupts activity to Pain wakes participant and disrupts activity; Pain wakes child from sleep to Pain wakes participant from sleep
 - xi. C20156 Mitochondrial disease current abdominal pain reason
 1. Revised: Other to Other, specify; The child tells me to The participant tells me
 - xii. C20161 Mitochondrial disease current abdominal pain duration type
 1. Revised: Until you/the child eats to Until the participant eats; Until you/the child falls asleep to Until the participant falls asleep; Until you/the child has a bowel movement to Until the participant has a bowel movement; Until you/the child passes gas to Until the participant passes gas; Until you/the child urinates to Until the participant urinates; Until you/the child vomits to Until the participant vomits
 - xiii. C20173 Mitochondrial disease prior abdominal pain reason
 1. Revised: Other to Other, specify; The child told me to The participant told me
 - xiv. C20187 Mitochondrial disease abdominal early fullness indicator
 1. Added: No; Yes
 - xv. C20200 Mitochondrial disease bowel movement frequency type
 1. Revised: Other to Other, specify; Requires Go Lightly by mouth or tube to Requires polyethylene glycol solution by mouth or tube
 - xvi. C20202 Mitochondrial disease bowel movement consistency result type
 1. Revised: Greasy to Greasy/oil droplets
 - xvii. C20215 Mitochondrial disease current medication type
 1. Added: Prucalopride (Motegrity)
 2. Revised: Other to Other, specify
 - xviii. C20220 Mitochondrial disease alternative medicine type
 1. Added: Energy therapies; Native American medicine; Other traditional forms of medicine; Traditional Chinese medicine
 2. Revised: Other to Other, specify
 - xix. C20225 Mitochondrial disease surgery type
 1. Added: Heart surgery
 2. Revised: Fundoplication (Nissen, Toupet) to Fundoplication (Nissen, Toupet, Thal, Dor)
 - xx. C20328 Mitochondrial disease bowel movements current medication type
 1. Added: Linaclotide, Plecanatide, Lubiprostone, Tenapanor; Prucalopride
 2. Revised: Other to Other, specify
12. Phosphorus Magnetic Resonance Spectroscopy (31P-MRS) F3090
- a. CDEs Added
 - i. C60184 Muscle group type
 - ii. C60185 Muscle group type other text
 - iii. C60186 Imaging 31 phosphorus magnetic resonance spectroscopy exercise protocol type
 - iv. C60187 Imaging 31 phosphorus magnetic resonance spectroscopy phosphocreatine depletion level measurement

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- v. C60188 Imaging 31 phosphorus magnetic resonance spectroscopy phosphocreatine spectra collect indicator
 - vi. C60189 Imaging 31 phosphorus magnetic resonance spectroscopy phosphocreatine recovery duration
 - vii. C60190 Imaging 31 phosphorus magnetic resonance spectroscopy ADP recovery duration
 - b. CDEs Removed
 - i. C20019 Imaging phosphorus magnetic resonance spectroscopy reproducibility indicator
 - ii. C20026 Imaging phosphorus magnetic resonance spectroscopy maximum ATP spectra assessment status
 - iii. C20027 Imaging phosphorus magnetic resonance spectroscopy maximum ATP spectra second assessment status
 - iv. C20028 Imaging phosphorus magnetic resonance spectroscopy exercise second duration
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C20025 Imaging 31 phosphorus magnetic resonance spectroscopy spectrum assessment status
 - 1. Added: No
 - 2. Removed: No, refused; No, unable
13. Pulmonary Function F3134
- a. CDEs Added
 - i. C60353 Pulmonary function test result not applicable status
 - ii. C60354 Forced vital capacity percent predict normal value
 - b. CDEs Removed
 - i. C02411 Laterality type
 - ii. C10177 Slow vital capacity percent of predicted normal value
 - iii. C11100 Pulmonary function test position type
 - iv. C11101 Pulmonary function test mouth apparatus type
 - v. C11104 Pulmonary function slow vital capacity (sVC) result value
 - vi. C11107 Pulmonary function peak expiratory flow result value
 - vii. C11110 Pulmonary function sniff nasal inspiratory pressure (SNIP) result value
 - viii. C11111 Pulmonary function sniff nasal inspiratory pressure (SNIP) peak pressure value
 - ix. C11112 Pulmonary function maximal voluntary ventilation (MVV) result value
 - x. C11114 Pulmonary function sniff nasal inspiratory pressure (SNIP) congestion indicator
 - xi. C17832 Pulmonary function maximum inspiratory pressure (MIP) type
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C11099 Pulmonary function test type
 - 1. Removed: Maximal Voluntary Ventilation; Peak Expiratory Flow; Slow Vital Capacity; Sniff Nasal Inspiratory Pressure
14. Reproductive and Hormonal History F3087
- a. CDEs Added
 - i. C59700 Pregnancy self or contribute sperm status
 - ii. C59701 Pregnancy other outcome comment text
 - iii. C59702 Polycystic ovarian syndrome diagnosis indicator
 - iv. C59703 Sex steroid deficiency cause type
 - v. C59708 Hormone therapy replace indicator
 - vi. C59712 Post-menopausal cause type other text
 - vii. C59714 Sex steroid deficiency diagnosis indicator
 - viii. C59715 Sex steroid receive indicator
 - b. CDEs Removed
 - i. C16167 Given birth or fathered a child indicator

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- ii. C16176 Hormone therapy indicator
 - iii. C19803 Dual X-ray absorptiometry scanner performed indicator
 - iv. C20003 Hypoglycemia diagnosis indicator
 - v. C20004 Hypoglycemia diagnosis type
 - vi. C20005 Hypoglycemia symptom diagnosis text
 - vii. C20006 Bone fracture indicator
 - viii. C20007 Bone fracture text
 - ix. C20008 Bone spine abnormal diagnosis indicator
 - x. C20009 Bone spine abnormal diagnosis text
 - xi. C20010 Dual X-ray absorptiometry scanner performed text
 - xii. C20011 Rickets diagnosis indicator
 - xiii. C20012 World Health Organization (WHO) Fracture Risk Assessment tool (FRAX) - fracture probability percentage value
 - c. Classification Changes
 - i. None
 - d. Permissible Value Modifications
 - i. C10981 Birth control method type
 - 1. Added: Hormonal IUD; Implantable hormonal device; Non-hormonal IUD; Oral contraceptives – estrogen/progestin pill
 - 2. Removed: Implantable devices with hormone; Oral contraceptives – combined pill
 - ii. C16169 Pregnancy outcome type
 - 1. Added: Other termination
 - 2. Removed: Therapeutic abortion or elective termination
 - iii. C16170 Menstrual period occurrence indicator; C16174 Menopause indicator
 - 1. Added: Unknown
 - iv. C16178 Post-menopausal cause type
 - 1. Added: Advancing age; Other, specify
 - 2. Removed: Natural
 - v. C20016 Hormone-related syndrome type
 - 1. Removed: Constitutional delay of growth and puberty; Hypogonadotropic hypogonadism; Polycystic ovary syndrome
15. Vital Signs F3094
- a. CDEs Added
 - i. C01507 Blood pressure diastolic measurement
 - ii. C01565 Blood pressure systolic measurement
 - iii. C01580 Temperature unit of measure
 - iv. C59706 Blood pressure cuff size unit of measure
 - v. C59709 Blood pressure cuff size value
 - vi. C59710 Temperature unit agnostic value
 - vii. C59711 Temperature measurement anatomic site other text
 - b. CDEs Removed (All except C01539 and C19565 were moved to the new Physical Exam CRF)
 - i. C01520 Head circumference measurement
 - ii. C01522 Height measurement
 - iii. C01523 Head circumference unit of measure
 - iv. C01539 Temperature measurement
 - v. C01541 Weight measurement
 - vi. C01581 Weight unit of measure
 - vii. C01582 Height unit of measure
 - viii. C11131 Body mass index value
 - ix. C15900 Weight percentile value

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- x. C15901 Height percentile value
 - xi. C19565 Blood pressure measurement
 - xii. C19571 Body mass index category
 - xiii. C19572 Height pediatric measurement
 - xiv. C19575 Length infant measurement
 - xv. C19577 Length infant unit of measure
 - xvi. C19579 Weight length infant measurement
 - xvii. C19580 Weight/Length percentile value
 - xviii. C19581 BMI Percentile Value
 - xix. C19582 Tanner stage pubic hair scale
 - xx. C19583 Tanner stage genitalia scale
 - xxi. C19608 Length percentile value
 - xxii. C19613 Length Z score
 - xxiii. C19616 Length standard infant use type
 - xxiv. C19617 Height Z score
 - xxv. C19618 Height standard infant use type
 - xxvi. C19619 Weight length Z Score
 - xxvii. C19620 Weight length standard infant use type
 - xxviii. C19621 BMI Z score
 - xxix. C19622 BMI standard infant use type
 - xxx. C19623 Head circumference percentile value
 - xxxi. C19624 Head circumference Z score
 - xxxii. C19625 Head circumference standard infant use type
 - xxxiii. C19631 Weight pediatric measurement
 - xxxiv. C19632 Weight pediatric unit of measure
 - xxxv. C19633 Height pediatric unit of measure
 - xxxvi. C19634 Body mass index pediatric value
- c. Classification Changes
- All CDEs: Supplemental – Highly Recommended (v1.0) to Supplemental (v2.0)
- i. C01519 Vital signs date and time
 - ii. C01521 Heart rate
 - iii. C01535 Respiratory rate
 - iv. C01550 Temperature measurement anatomic site
 - v. C01553 Blood pressure measurement position type
- d. Permissible Value Modifications
- i. C01550 Temperature measurement anatomic site
 - 1. Added: Forehead Cutaneous Infrared
 - 2. Removed: Bladder; Brain; Esophageal
 - ii. C01553 Blood pressure measurement position type
 - 1. Removed: Unknown

Removed CRFs (2)

1. Genetics Testing Clinical Diagnostics F1871
2. Genetics Testing Short Form F1870

These CRFs were replaced by the new Primary Mitochondrial Disease (PMD) Genetics CRF adapted from the NINDS CDE Parkinson's Disease v2.0 Genetics CRF, which includes CDEs from the Mito v1.0 CRFs.

New CRFs (14)

1. Bone Health History F3120
2. DXA F3129

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3. Exercise Wearables F3124
4. Family History F3121
5. Head Computed Tomography (CT) F3130
6. Hearing Loss in Mitochondrial Disease F3126
7. Labs of Bone Mineral Metabolism F3122
8. Magnetic Resonance Spectroscopy (MRS) F3131
9. Medical History F3125
10. Physical Exam F3095
11. Primary Mitochondrial Disease (PMD) Genetics F3133
12. Spine Magnetic Resonance Imaging (MRI) F3132
13. Staged Exercise Tolerance Test F3128
14. Vestibular Function in Mitochondrial Disease F3127

The following instruments were reclassified, removed, or newly added. Information in the instrument summaries was also updated as necessary. There were no Core instrument recommendations for Mito v1.0, and none were reclassified or added as Core for v2.0.

Updated Instrument Classifications (12)

Instrument	V1.0 Classification	V2.0 Classification
Beck Anxiety Inventory (BAI)	Supplemental	Supplemental – Highly Recommended
Center for Epidemiologic Studies-Depression Scale (CES-D)	Supplemental	Supplemental – Highly Recommended
Child Behavior Checklist (CBCL)	Supplemental	Supplemental – Highly Recommended
Delis-Kaplan Executive Function System (D-KEFS)	Supplemental	Supplemental – Highly Recommended
EuroQoL-5 Dimension Questionnaire (EQ-5D)	Exploratory	Supplemental – Highly Recommended
Generalized Anxiety Disorder (GAD-7)	Supplemental	Supplemental – Highly Recommended
International Pediatric Mitochondrial Disease Score (IPMDS)	Exploratory	Supplemental
Motor Function Measure (MFM)	Exploratory	Supplemental – Highly Recommended
Newcastle Mitochondrial Disease Adult Scale (NMDAS)	Supplemental	Supplemental – Highly Recommended
Peabody Developmental Motor Scale Second Edition (PDMS-2)	Supplemental – Highly Recommended	Supplemental
Quality of Life in Neurological Disorders (Neuro-QOL)	Supplemental	Supplemental – Highly Recommended
Short Form 36-Item Health Survey (SF-36)	Supplemental	Supplemental – Highly Recommended

Instruments Removed (19)

1. Adaptive Behavior Assessment Scale (ABAS-II)
2. Alberta Infant Motor Scale
3. Axon Sports Computerized Cognitive Assessment Tool (CCAT)
4. Child Depression Inventory (CDI)

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5. Comprehensive Assessment of Spoken Language (CASL)
6. Craig Handicap and Assessment Reporting Technique (CHART-SF) - Interview version
7. Craig Handicap and Assessment Reporting Technique (CHART-SF) - Paper version
8. Diagnostic and Statistical Manual of Mental Disorders (DSM-5)
9. Family Strain Questionnaire Assessment of Preschooled Children's Participation
10. Manual Muscle Testing-Using the Medical Research Council Muscle Grading Scale
11. Memory Assessment Scale
12. Peabody Picture Vocabulary Test 4th Edition (PPVT-4)
13. Physical Activity Questionnaire for Adolescents (PAQ-A)
14. Reynolds Intellectual Assessment Scale (RIAS)
15. Social Responsiveness Scale (SRS)
16. Vineland Adaptive Behavior Scales, Second Edition (Vineland-II)
17. Wechsler Abbreviated Scale of Intelligence (WASI)
18. Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III)
19. World Health Organization Quality of Life Assessment (WHOQOL-BREF)

New Instrument Recommendations (37)

Instrument	Subdomain	V2.0 Classification
Differential Ability Scales-II (DAS-II)	Academic Achievement	Supplemental
Wechsler Individual Achievement Test-4 (WIAT-4)	Academic Achievement	Supplemental
Sensory Organization Test (SOT)	Audiology	Exploratory
Zarit Burden Interview (ZBI)	Caregiver Reported Outcomes	Supplemental – Highly Recommended
Mini-Mental State Examination (MMSE)	Cognitive	Supplemental
NEPSY-II	Cognitive	Supplemental
Repeatable Battery for Assessment of Neuropsychological Status (RBANS)	Cognitive	Supplemental
Symbol Digit Modalities Test	Cognitive	Supplemental
Ask Suicide-Screening Questions (ASQ) Toolkit	Emotional/Behavioral	Supplemental
Beck Youth Inventories - 2nd Edition (BYI-II)	Emotional/Behavioral	Supplemental – Highly Recommended
Behavior Assessment System for Children, Third Edition (BASC-3)	Emotional/Behavioral	Supplemental – Highly Recommended
Hospital Anxiety and Depression Scale (HADS)	Emotional/Behavioral	Supplemental
Behavior Rating Inventory of Executive Function - Adult Version (BRIEF-A)	Executive Functioning	Supplemental – Highly Recommended
Tower of London-Drexel University (TOLDX): 2nd Edition	Executive Functioning	Supplemental
Trail Making Test	Executive Functioning	Supplemental
Fatigue Severity Scale (FSS)	Fatigue	Supplemental – Highly Recommended
Modified Fatigue Impact Scale (MFIS)	Fatigue	Supplemental – Highly Recommended
Reynolds Intellectual Assessment Scale, Second Edition (RIAS-2)	Intellectual Functioning	Supplemental
Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II)	Intellectual Functioning	Supplemental

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Instrument	Subdomain	V2.0 Classification
Wechsler Preschool and Primary Scale of Intelligence (WPPSI-IV)	Intellectual Functioning	Supplemental – Highly Recommended
Comprehensive Assessment of Spoken Language, Second Edition (CASL-2)	Language	Supplemental
Controlled Oral Word Association Test (COWAT) Subtest of the Multilingual Aphasia Examination (MAE)	Language	Supplemental
Peabody Picture Vocabulary Test 5th Edition (PPVT-5)	Language	Supplemental
Brief Visuospatial Memory Test Revised (BVRT-R)	Memory	Supplemental
Child and Adolescent Memory Profile (ChAMP)	Memory	Supplemental
Rey Auditory Verbal Learning Test (RAVLT)	Memory	Supplemental
Rey Complex Figure Test and Recognition Trial (RCFT)	Memory	Supplemental
Wide Range Assessment of Memory and Learning, Third Edition (WRAML-3)	Memory	Supplemental
12 Minute Walking Test	Motor Function	Supplemental
Grooved Pegboard Test	Motor Function	Supplemental
Mitochondrial Myopathy Composite Assessment Tool (MM-COAST)	Motor Function	Supplemental – Highly Recommended
Primary Mitochondrial Myopathy Symptom Assessment (PMMSA)	Motor Function	Supplemental
Purdue Pegboard	Motor Function	Supplemental
12-Item Short Form Health Survey (SF-12)	Quality of Life/Patient Reported Outcomes	Supplemental – Highly Recommended
Newcastle Mitochondrial Quality of Life Measure (NMQ)	Quality of Life/Patient Reported Outcomes	Supplemental – Highly Recommended
Epworth Sleepiness Scale (ESS) - Adult Version	Sleep	Supplemental
Test of Visual Perceptual Skills - 4th Edition (TVPS-4)	Visual-Spatial Processing	Supplemental

January 2020 Revisions

- General Core CRF updated to replace 'Gender' question with 'Sex assigned at birth' and 'Gender identity'.
- Two new CDEs added to CRF: C58676 (Birth sex assigned type) and C58677 (Gender identity type). C00035 has been removed.
- Start-Up document updated to reflect these changes.

June 2017 Revisions

- F1931 Mitochondrial and Gastrointestinal Diseases Assessment CRF updated based on Working Group member revisions

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February 2017 Revisions

- Mitochondrial Disease Highlight Summary updated on website.

December 2016 Revisions

- Working Group Summary documents updated on website:
 - Cognitive/Behavioral/Psychological
 - Biomarkers
 - Endocrinology/Diabetes/Gastrointestinal/Nutrition
 - Genetics
 - Imaging
 - Patient Reported Outcomes/QoL
 - Vision
 - Exercise Physiology
 - Neurological Assessments

May 2015 Revisions

- Classification of Supplemental – Highly Recommended identified on the CRFs for Genetics Testing Short Form and Genetics Clinical Diagnostics Form.
- Newcastle Mitochondrial Disease Pediatric Scale is Supplemental-Highly Recommended for Exercise Physiology Working Group. This was updated in the Notice of Copyright document and in the Working Group Summary.

April 2015 Revisions

- Updated Dr. Ellen Grober's email address in the AMnART document.
- Changed CDE Names having headline capitalization to sentence capitalization for CDEs on Genetics Testing forms.
- Corrected a URL for a file that was not opening in Mitochondrial Disease Biomarker CRF.
- Inserted additional reference on the 6 Minute Walk Test file.

March 2015 Revisions

- The Start-Up Resource Listings were revised.

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February 2015 Revisions

- Version 1.0 of Mitochondrial Disease CDEs posted.

January 2015 Revisions

- Changes to Mito roster:
 - correct spelling for Dr. Tanja Taivassalo and Dr. Mark Tarnopolsky
 - display correct institution for Dr. Anne Lombes
 - Display Dr. Bruce Cohen as Co-Chair of the Neurological Assessments Working Group