

**NINDS CDE Notice of Copyright**  
**The Newcastle Pediatric Mitochondrial Disease Scale (NPMDS)**

<b>Availability:</b>	Freely available: <a href="#">The Newcastle Pediatric Mitochondrial Disease Scale</a>
<b>Classification:</b>	<b>Supplemental-Highly Recommended:</b> Mitochondrial Disease for exercise physiology studies. Supplemental for all other Mitochondrial Disease studies.
<b>Short Description of Instrument:</b>	<p>The NPMDS has been introduced to allow evaluation of the progression of mitochondrial disease in patients less than 18 years of age. There are three age-specific versions of the NPMDS, 0-24 months, 2-11 years and 12-18 years. (The Newcastle Mitochondrial Disease Scale (NMDS) provides a similar assessment tool for adult patients). In the pediatric population, demonstrating a genetic or biochemical basis for mitochondrial disease can be very difficult. Consequently we would recommend that the scale be administered to patients where there is a strong clinical suspicion of mitochondrial disease as well as those with a confirmed (biochemical or genetic) diagnosis. Repeated administration of the scale permits the longitudinal monitoring of these patients.</p> <p>The aim of the disease rating scale is to standardize patient assessment and ensure accurate data collection. This information will provide an invaluable resource to help us understand the natural history of mitochondrial disease in children. The rating scale encompasses all aspects of mitochondrial disease by exploring several domains: Current Function; System Specific Involvement; Current Clinical Assessment and Quality of Life.</p>
<b>Scoring Information:</b>	<p><b>Scoring:</b> For sections I-III Each question is scored from 0-3 (0 representing normal, 1- mild, 2- moderate and 3- severe. In each case, examples of mild, moderate and severe impairment or disability are given), except for development which is scored between 0 and 7. Each of the first 3 section scores are calculated by simply summing the scores obtained for each question in that section. Higher scores reflect more severe disease.</p> <p>For section IV Each question is scored from 0-4. The responses are ordered from poorest quality of life on the furthest left- this scores 4, through to most desirable quality of life on the furthest right- this scores 0.</p> <p>A quality of life score derived from a <i>parent-completed questionnaire only</i> is calculated as follows: The 'raw score' is the sum of the scores obtained for all of the questions; The 'proportion score' is calculated by dividing the raw score by the maximum score for that age-specific scale i.e. 48 for 0-24 months and 60 for 2-11 and 12-18 years; The 'final score' (given to one decimal place) is calculated by multiplying the proportion score by 25.</p> <p>i.e. Final score = (raw score/total possible score) x 25</p>
<b>Comments / Special Instructions</b>	<p>There is a detailed manual available with instructions on how to score and adherence to the rules for scoring is required for the tool to function properly.</p> <p><b>Limitations for use in mitochondrial disease patients:</b> Possibly the complexity is too great to make this a universally applicable tool.</p> <p><b>Advantages for use in mitochondrial disease patients:</b> Similar to the NMADS, this is a global instrument that reflects the multi-system nature of mitochondrial disease.</p>

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<b>Rationale/ Justification:</b>	<p><b>Strengths/Weaknesses:</b></p> <p>Strengths include:</p> <ol style="list-style-type: none"><li>1. Assessment tool that can plot the temporal course of the disease</li><li>2. Semi-quantitative rating scale; multi-dimensional and reproducible</li><li>3. Progression of disease can be objectively monitored</li></ol> <p>It is predicted that the scale will also prove to be a useful tool for future clinical assessment of proposed treatments.</p> <p>This instrument has been used in several mitochondrial disease trials already: EPI-743, pyruvate therapy.</p> <p>Time consuming: - To maximize the consistency of administration of the NPMDS it is essential that all clinicians using the scale closely adhere to the instructions provided in the scale manual (8 pages). Individual interpretation of the questions will alter the scores assigned and have important consequences for the consistency and reliability of the data collected. - For the System specific involvement: This section rates function according to the patient and/or caregiver interview, clinician's knowledge of the patient and the clinical notes (notes must be consulted if there is any doubt about the most appropriate score) 4) Final score is complicated to calculate (raw score then mean of proportion score then final score each with multiplications and divisions) 5) No translation in multiple languages.</p> <p><b>Limitations:</b></p> <p>Rater qualification issues: - In all cases is it important to compare the patient's development and functional abilities to those expected from a child of that age. Due to the necessity of this baseline knowledge, the NPMDS should be administered by pediatricians, preferably with experience in mitochondrial disease.</p> <p>Recall issues: - For the patient "current function" Responses to all questions should be considered with appropriate regard for age. Each enquiry should take into account the situation for the preceding two week period for the 0-24 months scale and four week period for the 2-11 and 12-18 years scales. - For the System specific involvement: Each enquiry should take into account the situation for the preceding six month period for the 0-24 months and 2-11 years scales and the preceding 12 months for the 12-18 scale, unless otherwise stated in the question.</p> <p><b>Advantages:</b></p> <p>Provides a global assessment of the clinical severity of mitochondrial disease, including patient quality of life issues</p>
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<p><b>Rationale/Justification</b></p>	<p><b>Psychometric Properties:</b> To maximize the consistency of administration of the NPMDS it is essential that all clinicians using the scale closely adhere to the instructions provided in this manual. Individual interpretation of the questions will alter the scores assigned and have important consequences for the consistency and reliability of the data collected.</p> <p><b>Administration:</b> There are three age-specific versions of the NPMDS, 0-24 months, 2-11 years and 12-18 years. In all cases it is important to compare the patient's development and functional abilities to those expected from a child of that age. Due to the necessity of this baseline knowledge, the NPMDS should be administered by pediatricians, preferably with experience in mitochondrial disease. We advise that the scale should be completed at least every six months for children under the age of two and at 6-12 month intervals for older children.</p>
<p><b>References:</b></p>	<p>Phoenix C, Schaefer AM, Elson JL, Morava E, Bugiani M, Uziel G, Smeitink JA, Turnbull DM, McFarland R. A scale to monitor progression and treatment of mitochondrial disease in children. <i>Neuromuscul Disord.</i> 2006 Dec;16(12):814-20. Epub 2006 Nov 22.</p> <p>Fujii T, Nozaki F, Saito K, Hayashi A, Nishigaki Y, Murayama K, Tanaka M, Koga Y, Hiejima I, Kumada T. Efficacy of pyruvate therapy in patients with mitochondrial disease: a semi-quantitative clinical evaluation study. <i>Mol Genet Metab.</i> 2014 Jun;112(2):133-8. doi: 10.1016/j.ymgme.2014.04.008. Epub 2014 May 2.</p> <p>Blankenberg FG, Kinsman SL, Cohen BH, Goris ML, Spicer KM, Perlman SL, Krane EJ, Kheifets V, Thoolen M, Miller G, Enns GM. Brain uptake of Tc99m-HMPAO correlates with clinical response to the novel redox modulating agent EPI-743 in patients with mitochondrial disease. <i>Mol Genet Metab.</i> 2012 Dec;107(4):690-9. Epub 2012 Sep 28. PMID:23084792</p> <p>Martinelli D, Catteruccia M, Piemonte F, Pastore A, Tozzi G, Dionisi-Vici C, Pontrelli G, Corsetti T, Livadiotti S, Kheifets V, Hinman A, Shrader WD, Thoolen M, Klein MB, Bertini E, Miller G. EPI-743 reverses the progression of the pediatric mitochondrial disease--genetically defined Leigh Syndrome. <i>Mol Genet Metab.</i> 2012 Nov;107(3):383-8. Epub 2012 Sep 10.</p>