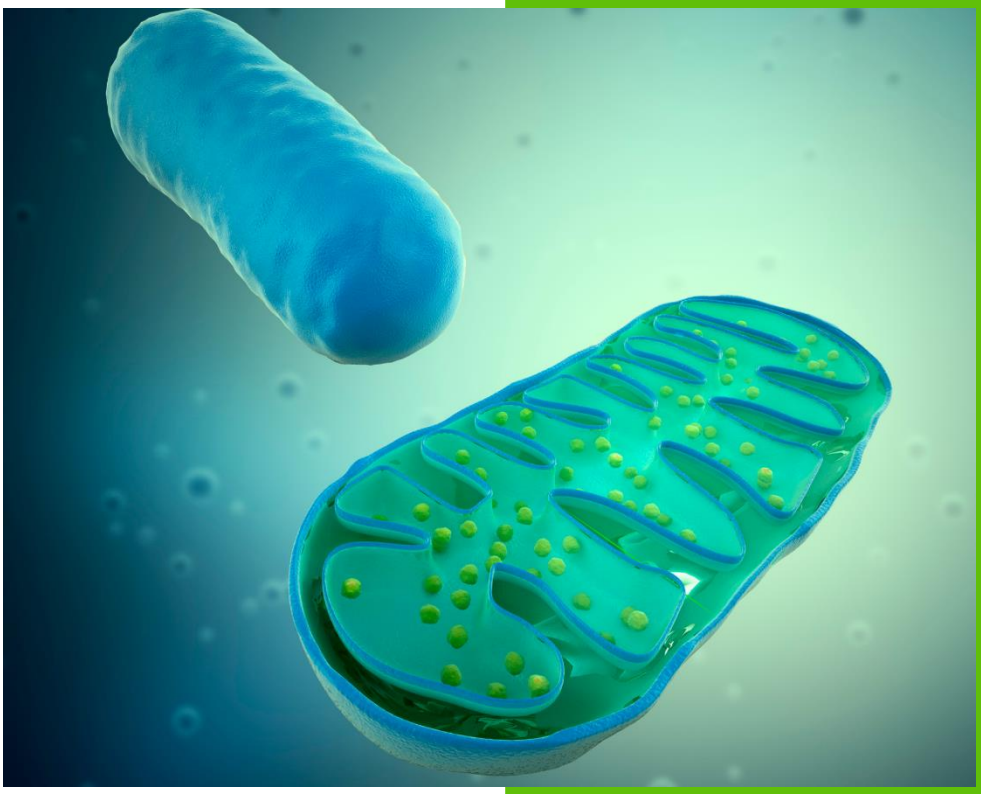
SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Bologna

Istituto delle Scienze Neurologiche
Istituto di Ricovero e Cura a Carattere Scientifico

2025

List of Outcomes

# Project COS-MNGIE

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# Core Outcome Set in Mitochondrial Neurogastrointestinal Encephalomyopathy



The project **Core Outcome Set in Mitochondrial Neurogastrointestinal Encephalomyopathy (COS-MNGIE)** aims to develop a set of health outcomes (Core Outcome Set, or COS)[1], relevant for clinicians and for people with MNGIE, that should be adopted as a minimum in clinical practice and in research on the efficacy, safety and value of treatments, including current and future permanent enzyme-replacement treatments.

To develop the Core Outcome Set, we adopted a multi-phase, consensus-driven methodology designed to integrate scientific evidence with the perspectives of clinicians and people with MNGIE.

The project stemmed from a foundational position paper on MNGIE[2]. In 2022 a Scientific Advisory Group (SAG) including key stakeholders (clinical experts, researchers and a person with lived experience of MNGIE) committed to define a preliminary list of 21 relevant outcomes developed from the conclusions of the position paper, enriched by an updated scoping review of the available literature. Consensus on core outcomes by key clinical experts was reached through a two-round Delphi process. At the same time, a focus group was conducted by the MITOCON Advocacy Group to inform the content of a global survey aimed at identifying health and wellbeing domains and outcomes most meaningful to people living with MNGIE. Relevant outcomes identified by people with MNGIE and by clinical experts were publicly shared during an open final consensus meeting held online on July 11th, 2025. Remaining uncertainties were discussed and resolved. The meeting of the COS-MNGIE project brought together 36 participants, including clinicians, researchers, people with MNGIE and advocacy groups involved in the care and study of MNGIE.

Detailed information about the project is available in the published protocol on Zenodo[3].

[1] Core Outcome Measures in Effectiveness Trials: https://www.comet-initiative.org/
[2] Hirano M, Carelli V, De Giorgio R *et al*. Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE): Position paper on diagnosis, prognosis, and treatment by the MNGIE International Network. J Inherit Metab Dis. 2021;44(2):376-387. doi:10.1002/jimd.12300
[3] https://zenodo.org/records/7900200#.ZFUI8WgzaUk

## List of Core Outcomes

This list of outcomes has been finalized during a consensus meeting held online on July 11, 2025.

| OUTCOME | SUGGESTED MINIMUM ASSESSMENT TIMINGS * |
|---|---|
| **Thymidine (dThd) and deoxyuridine (dUrd)** | For OLT and AHSCT: monthly for 2-6 months |
| **Hepatic function** | For OLT and AHSCT: monthly for 2-6 months |
| **Type of nutrition** | Every 6 months |
| **Body weight** | Every 3 months |
| **Gastro-intestinal symptoms** | Every 3 months |
| **Abdominal pain** | Every 3 months |
| **Nausea/vomiting** | Every 3 months |
| **Diarrhoea** | Every 3 months |
| **Neurological assessment** | Timing depending on specific neurological manifestations |
| **Polyneuropathy** | After 6 months, and subsequently every year |
| **Functional disability symptoms** | After 6 months, and subsequently every year |
| **Survival** | |
| **Fatigue** | After 6 months, and subsequently every year |
| **Thymidine phosphorylase (TP)** [§] | For OLT: Yearly (>6 months after transplantation) [#] |
| | For AHSCT: Monthly (2-6 months after transplantation) |
| **Body composition trajectory** [¶] | Every six 6 months |
| **Ophthalmoparesis** | After 6 months, and subsequently every year |
| **Hearing** | After 12 months, and subsequently every year |
| **Leukoencephalopathy** | After 12 months, and subsequently every year |
| **Quality of Life (QoL) in MNGIE patients (SAVEQoL instrument)** | After 6 months, and subsequently every year |

AHSCT = Allogeneic hematopoietic stem cell transplantation. OLT = orthotopic liver transplantation. * Suggested assessment timings are intended after permanent enzyme-replacement treatment (those available at the time of the development of this COS are OLT and AHSCT). § The biological sample where TP activity is measured must be carefully chosen depending on what therapy (and to what target tissue) is being monitored. # TP activity in blood samples is expected to be unchanged after OLT, and therefore uninformative about the efficacy of the enzyme-replacement treatment. ¶Body composition assessed by means of any available method.

**Scientific Advisory Group (SAG)**: Matteo Cescon (clinical expert), Michio Hirano (clinical expert), Carolina Malagelada (clinical expert), Ramon Martí (expert biochemist), Serena Massucci (advocacy group), Francesco Nonino (methodologist), Silvano Pioli (person with MNGIE), Rita Rinaldi (clinical expert), Agathe Roubertie (clinical expert). **Project Management Group**: Flavia Baccari, Elisa Baldin, Claudia De Santis, Francesco Nonino, Rita Rinaldi, Martino Schettino, Luca Vignatelli. **Participants to the consensus process**: Elisa Baldin, Bridget E Bax, Enrico Bertini, Elisa Boschetti, Valerio Carelli, Carlo Casali, Matteo Cescon, Hazel Currie, Roberto D'Angelo, Roberto De Giorgio, Claudia De Santis, Daria Diodato, Massimiliamo Filosto, Sema Kalkan, Costanza Lamperti, Austin Larson, Cecilia Marelli Tosi, Ramon Martí, MNGIE India, Kira Mann, Maria Cristina Morelli, Olimpia Musumeci, Francesco Nonino, ORDI (Organization for Rare Diseases India), Silvano Pioli, Alessia Pugliese, Shamima Rahmam, Rita Rinaldi, Agathe Roubertie, Fernando Scaglia, Martino Schettino, Manuel Schiff, Vincenzo Stanghellini, Jelle van den Ameele, Luca Vignatelli, Irina Zaidman. **MNGIE survey translation**: Kaoutar Ouabicha, Judith Pantenburg, Amina Taguirov.