A retrospective natural history study of subjects affected by Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE): frequently asked questions (FAQs)

Frequently asked questions (FAQs)

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Questions about the study

- **What is the study about?**

MNGIE (Mitochondrial Neuro-Gastro-Intestinal Encephalomyopathy) is an ultra-rare mitochondrial disease, caused by mutations in the TYMP gene. Innovative treatment strategies are emerging for MNGIE, including gene therapies and other advanced medicinal therapies. Some of these will soon be tested in clinical trials. However, a comprehensive and up-to-date natural history study of MNGIE will be crucial to inform the design of these clinical trials and to select appropriate clinical and biochemical outcome measures.

This natural history study aims to include the clinical information of as many people affected by MNGIE as possible. Recruitment to the study is worldwide, and will include both published and unpublished patients, as well as patients who are already part of other disease registries, who have passed away, or who have received treatments like liver or bone marrow transplantation.

The study aims to understand clinical progression and identify biochemical, molecular, histological, and histochemical parameters that can help in early diagnosis, improve prognosis, and assess therapeutic outcomes.

- **I am a patient and would like to be included in the study. How do I do this?**

If you or someone in your family is affected by MNGIE, and you would like your clinical data to be included in this study, feel free to share this information with your treating clinician. They can then contact the study team, who will share a link to the survey with them.

- **I am a clinician and would like my patient to be included in the study, how do I do this?**

We are looking for clinicians who follow/have followed patients affected by MNGIE, either in a clinical or in a research setting, and who would be willing to share anonymised clinical information via an online secure survey. Please contact the study team for further information and to share a link for the study survey.

The study is focusing on patients with MNGIE, caused by mutations in the TYMP gene. At this time, we are not considering other genetic aetiologies of MNGIE.

- **Can I include several members of the same family?**

Yes, we welcome information from multiple members within the same family. A new entry in REDCap (see 'Where will the data be stored?' question for further details) will need to be completed for each family member. Family History information will be collected within the family history section of the survey.

- **Can I include asymptomatic patients?**

Yes, we welcome information from patients who are currently asymptomatic, carrying recessive variants in the TYMP gene.

- **Can I include paediatric patients?**

Yes, patients of any age can be included in the study.

- **I am a clinician who used to care for a patient with MNGIE. Can they still be included in the study?**

Yes, we are interested in finding out as much information about this disease as we can, so welcome information about patients who are not under your care anymore or have unfortunately passed away. If someone is not under your care anymore, it might be worth reaching out to the clinician currently caring for the patient to prevent duplication of efforts.

Questions about the online survey

- **How long will it take to complete the online survey?**

Completing the survey will take approximately 30 minutes to 1 hour per patient.

- **Will all data be anonymous?**

Yes, the survey will not ask for any identifiable information about the patient. For example, the survey will not ask for the patient's name, address, contact details, or hospital numbers. Collection of dates (for example, date of birth, date of diagnosis, date of a major intervention) has been reduced to month and year or just the year.

- **Where will the data be stored?**

Anonymous data will be collected in a secure REDCap database through an online questionnaire/survey. The survey should be completed by a clinician or their delegates.

All data will be stored in a secure environment at the University of Cambridge (United Kingdom).

- **Which type of information do I need to prepare before starting the survey?**

The survey has been designed to capture the following information, summarised in the table below. All information collected will help us build the natural history of patients with MNGIE.

Demographics	**Medical history and diagnostic information**	**Genetics and histology**
Demographics: Partial date of birth or current age, biological sex, ethnicity, country of origin/birth	Year of MNGIE diagnosis	Type and year of genetic testing
Lead clinician/center – center name & clinician contact (email)	Year of symptom onset	Mutation, ideally at the cDNA level and the protein level
Registry information, including ID number if the patient is already included in a registry.	Other medical conditions	Histology/histochemistry and molecular data
Previous publication status	First specialist seen by the patient	
Family history	First specialist suspecting/diagnosing MNGIE	
Consanguinity	Misdiagnosis (if applicable)	
Patient status – alive?		
Clinical features	**Laboratory tests and other diagnostic investigations**	**Major interventions and treatments**
Main clinical features and year of onset	Laboratory tests performed, including approximate date	Major interventions (bone marrow transplantation, liver transplantation, etc.)
	Plasma and urine dThd and dUrd measurements	
	Mitochondrial biomarkers	
	Functional/cognitive scales	
	Technical investigations (ENG/EMG/EEG/MRI…)	

- **Can I return to the survey if I completed only part of it?**

Yes, it is possible to return to the survey if it cannot be completed in one go. REDCap has a 'Save & Return Later' function that will need to be used for this to be possible. Further information on how this can be done will be provided. Once submitted, the survey cannot be edited anymore, but please do not hesitate to reach out to the study team with any concerns.

- **What do I need to do if I experience any technical difficulties with the online survey?**

Please contact the study team via email: add-tr.mitoteam@nhs.net

Study Results

- **How do I find out about the results of the study?**

Data for this study will be collected during the course of 2026. During this period and afterwards, the study team will collate and analyse all the data. The results of the study will be published, and a lay summary of the results will be prepared and shared with the contributing clinicians and via any involved patient organisations.

Questions about ethics and regulatory approvals

- **Has this study received ethics approval?**

Yes, the study has received approval from the Human Biology Research Ethics Committee of the university of Cambridge. The study is conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (ICH-GCP) guidelines.

- **Do clinicians need local ethics approval to contribute to data collection?**

Ethical and regulatory requirements differ between countries and institutions. Before entering data into the study database, clinicians are asked to confirm that they comply with their local ethical and regulatory requirements and that they have the appropriate approvals or permissions to share anonymised data.

- **Is patient consent required?**

Consent requirements depend on local regulations and the type of consent already obtained at each site. In some centres, patients may already have consented to research and sharing of anonymised clinical data through registries or previous studies, and this may allow their data to be included without additional consent, depending on local ethical approvals.

Study team

- **Who are the people conducting the study?**

The study is led by a team of clinical researchers at the University of Cambridge (United Kingdom) and the University of Bologna (Italy). The principal investigators are Dr Jelle van den Ameele and Prof. Caterina Garone, who are both clinical neurologists with extensive experience looking after patients with mitochondrial disease, including patients and families affected by MNGIE. They are developing novel treatments for these conditions, for which good natural history study data are essential.

More information about the study team in Cambridge can be found on their website: https://mitocamb.medschl.cam.ac.uk.

- **How is the study funded?**

The study is funded through an agreement with Pierrepont Therapeutics (http://www.pierreponttx.com), a company who are currently developing an innovative treatment for MNGIE. The company will have access to the (anonymous) data to help them improve treatment, develop better protocols for clinical trials in MNGIE, and ultimately work towards approval of better and safer treatments for MNGIE.

The funder will not have exclusive access to the data. Upon publication of the study, the protocol, data, and results will be publicly available to all clinicians and researchers with an interest in developing treatments for MNGIE, to benefit the entire research community and all patients affected by MNGIE and mitochondrial disease.

- **I would like to contact the study team; how do I do this?**

The study team can be contacted via email: add-tr.mitoteam@nhs.net, and will aim to respond within 3 working days.