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Leigh syndrome roadmap project: a natural history study (UK)

Submission date
14/05/2026

Recruitment status
Recruiting

Registration date
08/06/2026

Overall study status
Ongoing

Last Edited
08/06/2026

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Leigh Syndrome (LS) is a rare, progressive, genetic condition. It is associated with developmental regression (loss of previously acquired cognitive and motor skills) and muscle, movement and balance problems. Onset of LS generally occurs in early childhood; however, onset in adolescence and early adulthood has been observed. To date, over 110 genes have been identified to cause LS. There are currently no effective treatments for LS, the natural history of which is not well understood and has not been rigorously studied.
In this study, we want to find out more about Leigh Syndrome. We want to collect information about how people with Leigh Syndrome experience changes in their condition over time (we refer to this as natural history). This information will help doctors and researchers better understand the disease and support the development of future research studies.

Who can participate?
Patients aged under 75 years with a a diagnosis of Leigh Syndrome

What does the study involve?
Participants will attend study visits in Newcastle upon Tyne every 3–6 months, with some follow-up appointments possibly taking place by video or telephone. They will also complete questionnaires every 3 months, either online or on paper.
The study includes a range of assessments, some carried out by the research team and others completed by the patient or their caregiver. Many of these assessments are part of routine care. Study visits will take around 1–2 hours, and questionnaires around 30–60 minutes.

What are the possible benefits and risks of participating?
No direct benefit to participants can be guaranteed. However, the information collected may improve understanding of Leigh syndrome and support future research into treatments for Leigh syndrome and other mitochondrial diseases.

Where is the study run from?
The Newcastle upon Tyne Hospitals NHS Foundation Trust (Newcastle Hospitals) (UK)

When is the study starting and how long is it expected to run for?
March 2026 to March 2029

Who is funding the study?
The Leigh Syndrome International Consortium

Who is the main contact?
Isabel Barrow, nuth.mitoresearch@nhs.net

Contact information

Type(s)
Scientific, Public

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Additional identifiers

Integrated Research Application System (IRAS)
331565

Central Portfolio Management System (CPMS)
70571

Study information

Scientific Title

Leigh syndrome roadmap project: a natural history study (UK)

Acronym
LSRP

Study objectives
The primary objective of this study is to define the natural history of Leigh syndrome spectrum disorders (LSS) through objective and subjective assessments of symptom involvement over time, including:
1. Objective clinician assessments of movement, dystonia, ataxia and mitochondrial disease burden
2. Subjective measures of fatigue, quality of life (QoL), function, daily sign and symptom observation, and caregiver burden.

The secondary objective is to evaluate medical history-based objective outcome measures including respiratory function, cardiac function, acute decompensation and infection history, growth, hospitalizations, and other disease symptoms

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/12/2025, North East - Newcastle & North Tyneside 1 Research Ethics Committee (2nd Floor, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 25/NE/0179

Study design
Observational cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Leigh syndrome

Interventions
This study will involve 20 participants (aged between 0 and 75 years) with a genetically confirmed diagnosis of a Leigh syndrome spectrum (LSS) disorder. Each participant will be followed up for (up to) 3 years. Follow-up will be via in-person visits and remote assessments (video/telephone calls).

Participants will be identified and recruited via the NHS Highly Specialised Service for Rare Mitochondrial Disorders at the Newcastle upon Tyne Hospitals NHS Foundation Trust (Newcastle Mitochondrial Disease Clinic for Adults and Children) and via a number of other NHS secondary and tertiary care sites that will act as participant identification centres. Patients may also self-refer into the study in response to study adverts.

To be eligible to participate, participants will need a confirmed genetic diagnosis of LS (for this purpose, a genetics report from an NHS diagnostic laboratory stating the genetic diagnosis will be sufficient). Adults who lack the capacity to provide consent will be able to participate provided a suitable consultee can be identified and is of the opinion that the potential participant would wish to be involved.

The direct clinical care team at site (and at the PICs) will identify potential participants via screening of clinic lists. Potentially eligible patients will be sent a study invitation letter or will be contacted by telephone/in person by their direct clinical care team and provided with information about the study (via the Participant Information Sheet). Time to consider participation and the opportunity to discuss the study in detail with a member of the research team will be provided.

Interested potential participants will be contacted and their eligibility (based on medical history) ascertained by a member of the research team. Those who are deemed to be eligible based on this contact will be invited to attend a study baseline visit at site.

At the baseline visit, participants will be asked to provide written informed consent (or parental consent/the opinion of a consultee sought), and eligibility will be confirmed in writing. The following study assessments will then be conducted:
1. Collection of demographics, medical history and results from previous clinical tests
2. Newcastle Paediatric Mitochondrial Disease Scale (NPMDS) or Newcastle Adult Mitochondrial Disease Scale (NMDAS)
3. Barry Albright Dystonia Scale (BADS)
4. Movement Disorder Childhood Rating Scale
5. Scale for the Assessment of Ataxia (SARA)
6. Modified Fatigue Impact Scale (MFIS)
7. Paediatric Quality of Life Inventory (PedsQL)
8. Caregiver Burden Scale
9. Observer Reported Outcome (ObsRO)
10. Paediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT)

Participants will undergo follow-up assessments at intervals of 3-6 months following baseline until the end of the study. At these visits, the above assessments will be completed.

Participants who are not seen in-person at such regular intervals will be asked to complete the following assessments remotely every 3 months:
1. MFIS
2. PedsQL
3. Caregiver Burden Scale
4. ObsRO survey (to continue daily for 1 week)

The overall study duration is 3 years. Participants may be recruited throughout this period and will be followed up until
the overall study end date. This means that the actual duration of per-participant follow-up will be variable and will be
up to 3 years.

Once the study is completed, participants will return to their usual clinical care.

Data from the study will be uploaded to the study REDCap database hosted by the Children's Hospital of Philadelphia (CHOP), USA.

This study is devised and funded by the Leigh Syndrome International Consortium; institutions in several countries are collecting similar data. Data from all countries (under separate protocols and regulatory permissions) will be combined for analysis.

Intervention Type
Other

Primary outcome(s)
1. Disease severity measured using the Newcastle Paediatric Mitochondrial Disease Scale (NPMDS) or Newcastle Mitochondrial Disease Adult Scale (NMDAS) at baseline and every 6 months for up to 3 years

2. Dystonia severity measured using the Barry Albright Dystonia Scale (BADS) at baseline and every 3–6 months for up to 3 years

3. Movement disorder severity measured using the Movement Disorder Childhood Rating Scale (MDCRS) at baseline and every 3–6 months for up to 3 years

4. Ataxia severity measured using the Scale for the Assessment and Rating of Ataxia (SARA) at baseline and every 6 months for up to 3 years

5. Fatigue measured using the Modified Fatigue Impact Scale (MFIS) at baseline and every 3 months for up to 3 years

6. Health-related quality of life measured using the Paediatric Quality of Life Inventory (PedsQL) at baseline and every 3 months for up to 3 years

7. Caregiver burden measured using the Caregiver Burden Scale at baseline and every 3 months for up to 3 years

8. Daily symptoms and function measured using the Observer Reported Outcome (ObsRO) survey at baseline and every 3 months for up to 3 years

9. Functional ability measured using the Paediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT) at baseline and every 3 months for up to 3 years

Key secondary outcome(s))
1. Respiratory function, cardiac function, growth, acute decompensation events, infection history, hospitalisations, and other disease-related clinical outcomes collected from medical records at baseline and throughout follow-up for up to 3 years
2. Acute adverse events (including metabolic decompensation, seizures, stroke and infections) recorded throughout the study period for up to 3 years

Completion date
01/03/2029

Eligibility

Key inclusion criteria

1. Be aged <=75 years at the start of study (baseline)
2. Have a genetically confirmed diagnosis of a Leigh syndrome spectrum (LSS) disorder
3. Be able to provide informed consent (consent on behalf of participants aged <16 years will be obtained from a parent/individual with parental responsibility)
or
4. For adult participants lacking mental capacity, have an appropriate consultee to provide their opinion on participation, in compliance with the Mental Capacity Act 2005. The consultee will be a family member, caregiver, or another individual who knows the participant well and can offer insights into their preferences, values, and best interests

Healthy volunteers allowed
No

Age group
All

Lower age limit
0 years

Upper age limit
75 years

Sex
All

Total final enrolment
0

Key exclusion criteria
Potential participants will not be eligible if they:
1. Have a genetic disease other than primary mitochondrial disease (e.g., Down syndrome), including genetic diseases with secondary mitochondrial dysfunction
2. Are unable, in the opinion of the recruiting investigator, to complete study assessments

Date of first enrolment
08/06/2026

Date of final enrolment
01/03/2029

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
England
NE7 7DN

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
The Leigh Syndrome International Consortium

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (the RedCAP instance at CHOP). The Newcastle data will be stored on the Trust RedCAP instance.
As indicated above, de-identified study data will be held by CHOP. This data will be held on the REDCap system, which has a number of security controls (e.g., limits to access and secure back-up). Any data exported from REDCap will be de-identified and downloaded to secure systems with restricted access. Sharing of de-identified datasets will only occur once relevant agreements and secure transfer arrangements are in place.
Data generated by the study will be combined with data from separate studies undertaken at a number of other sites internationally. Collation of these datasets will be via the study's REDCap database under the management of the Data Co-ordinating Centre at CHOP.
Participating members of the Leigh Syndrome International Consortium will be involved in analyses of the study dataset. The chief investigator for this study and other members of the UK research team will be involved in the data analyses and dissemination activities.
Identifiable personal data will not be included in the analyses of the study data or publication of

the results. The research team are used to working in a rare disease area and in reviewing publications prior to submission to ensure that, where small numbers are involved, identification of individuals is not possible.
De-identified data sets will be transferred from the local secure REDCap database via a Data Access Group (DAG) to the secure REDCap database hosted by CHOP. DAGs restrict viewing of data within a database so that each site can view data entered from their site but cannot view data from any other sites. Users at each site are assigned to a group and will only be able to see records created by users within their group.
Only staff working on the study at site or authorised members of the data co-ordinating centre at CHOP will have access to the study data on REDCap. This database has a full audit trail to show when and who access it and when any changes are made.
Publications resulting from this research will involve the aggregated analysis of data from multiple institutions collecting LS natural history study data. Participant data will remain confidential in any scientific publication or presentation.
Findings from the study may be reported at local, national and international meetings; on social media platforms (including but not limited to the Leigh Syndrome International Consortium and associated members, Newcastle University, and charity partners); as well as in peer-reviewed journals.
Study participants will be advised in the Participant Information Sheet that they can contact the research team to request a lay summary of the overall research results once the study is complete.
We will store our data for 20 years.
Patients consent to data sharing.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 2.1	20/01/2026	05/06/2026	No	No