

Long Covid and myalgic encephalomyelitis /chronic fatigue syndrome (ME/CFS) study

Submission date 15/04/2026	Recruitment status Recruiting	☐ Prospectively registered ☐ Protocol
Registration date 26/05/2026	Overall study status Ongoing	☐ Statistical analysis plan ☐ Results
Last Edited 26/05/2026	Condition category Other	☐ Individual participant data ☒ Record updated in last year

Plain English summary of protocol

Background and study aims:

People living with Long Covid and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) often experience longterm symptoms that affect daily life, work, and wellbeing. Many also struggle to access consistent care and support. The HERITAGE study aims to understand people's symptoms over time, their experiences of NHS and community services, and what makes care helpful or unhelpful. The study also aims to identify how services can be improved nationally, using feedback from patients, carers, and healthcare professionals.

Who can participate?

Four groups of adults aged 18 years and over can take part:

1. People with Long Covid
2. People with ME/CFS
3. People with both conditions
3. Healthcare professionals, care and individuals involved in supporting people with these conditions

Participants may be currently receiving specialist NHS care (at a participating clinic), have received care in the past, or may not be in specialist services. Some participants will also be invited to take part in an interview.

What does the study involve?

Participants with Long Covid or ME/CFS will be asked to complete questionnaires about their symptoms, daily activities, quality of life, and use of healthcare services. These can be completed online using the ELAROS 'Autonom-e' app/website or on paper.

Some participants, carers (when supporting a participant), and healthcare staff will be invited to take part in a onetoone interview to share their experiences of services, support, and recovery. These interviews can be done by phone, online (Microsoft Teams) or, where possible, in person. The study also includes a national Quality Improvement Collaborative, where NHS teams, patients, and researchers work together to understand challenges in current services and find ways to improve care.

No treatments, tests, or medicines are given as part of this study.

What are the possible benefits and risks of participating?

There may be no direct personal benefit, but participants may find it helpful to reflect on their experiences and contribute to research that could improve future care for people with Long Covid and ME/CFS.

Risks are minimal. Completing questionnaires or interviews may feel tiring or emotional for some people. Participants can take breaks, skip questions, or stop at any time. All information will be kept confidential.

Where is the study run from?

The study is led by the University of Leeds and run in collaboration with NHS Long Covid and ME/CFS services (in Leeds, Leicester, Hertfordshire and Cornwall) and partner universities (University of Leicester and Oxford) (UK)

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

May 2026 to December 2028

Who is funding the study?

The National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?

For any questions about the study, please contact the research team, heritage-studyteam@leeds.ac.uk

Contact information

Type(s)

Principal investigator, Scientific, Public

Contact name

Prof Manoj Sivan

Contact details

Leeds Institute of Rheumatic & Musculoskeletal Medicine (LIRMM)

Chapel Allerton Hospital

Leeds

United Kingdom

LS7 4SA

+44 (0)1133922564

M.Sivan@leeds.ac.uk

Additional identifiers

Study information

Scientific Title

Health Effects fRom Infection sequelae: Tailoring services and Advancing Guidance (HERITAGE) in Long Covid and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

Acronym

HERITAGE

Study objectives

HERITAGE aims to inform high-quality and cost-effective services for LC and ME/CFS. Below, we set out the research questions (RQ), objectives and key milestones for each of the three work packages (WPs).

WP1 (RQ1): What is the diagnostic overlap between the two conditions, what are the condition trajectories and long-term clinical outcomes in both conditions?

Objective 1a: Estimate the proportion of diagnostic overlap between LC and ME/CFS in people meeting the diagnostic criteria for each condition.

Objective 1b: Evaluate long-term clinical outcomes of LC and ME/CFS using a standard set of condition-specific outcome measures and health measures (EQ-5D-5L) in all participants (including a 'non-clinic' national cohort).

WP2 (RQ2): What is the clinical and cost-effectiveness of alternative service models for LC and ME/CFS?

Objective 2a: Assess the health and social care costs and societal costs in LC and ME/CFS.

Objective 2b: Evaluate the cost-effectiveness of specialist LC/ME/CFS services in comparison to a non-clinic national cohort.

WP3 (RQ3): How to improve the quality of care for LC and ME/CFS and develop a national service framework for both conditions?

Objective 3a: Produce longitudinal case studies of service staffing, skill set and multi-condition integration in four specialist service models

Objective 3b: Set up and run a Quality Improvement Collaborative (QIC) to address the effectiveness, equity, safety, patient-centredness and timeliness of services and staff skill sets for LC and ME/CFS. Develop training resources and a national service framework for both conditions, that will potentially be applicable to other post-infection conditions.

Ethics approval required

Ethics approval required

Ethics approval(s)

Submitted 20/03/2026, North West – Greater Manchester (GM) East Research Ethics Committee (Barlow House, 4 Minshull Street, Greater Manchester, M1 3DZ, United Kingdom; N/A; gmeast.rec@hra.nhs.uk), ref: 26/NW/0105

Primary study design

Observational

Secondary study design

Cohort study

Study type(s)

Health condition(s) or problem(s) studied

Long Covid and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

Interventions

The HERITAGE study will use a mixed methods design, combining quantitative and qualitative data from individuals with Long Covid (LC) and myalgic encephalomyelitis/chronic fatigue

syndrome (ME/CFS) recruited from four localitybased service models (Leeds, Leicester, Hertfordshire, and Cornwall) and a nonclinic national cohort of individuals who do not have access to specialist services.

The study will enrol approximately 3,000 individuals with LC and/or ME/CFS. Allowing for an estimated 50% attrition rate, we anticipate that over 1,500 participants will complete the 12month longitudinal followup, providing robust trajectories of symptoms, functioning, and service use over time. Quantitative data will include patientreported outcome measures, vocational outcomes, and health economic data, including patientborne and NHS costs, to support costeffectiveness analyses.

The qualitative work package will employ a combination of purposive and stratified sampling to ensure a representative and analytically robust sample across conditions, service models, and levels of service engagement. Up to 106 qualitative participants will be recruited in addition to the quantitative cohort. This will include:

Up to 52 people with LC or ME/CFS, comprising 32 participants recruited from the four specialist services (Leeds, Leicester, Hertfordshire, and Cornwall) and 20 participants not engaged with specialist services, recruited nationally. These participants may also form a sub-sample of the 3,000 quantitative participants.

Up to 24 healthcare professionals or staff providing, commissioning, or supporting LC or ME/CFS services across the four localities.

Participation in the Quality Improvement Collaborative (QIC) by up to 30 additional individuals, including people with LC or ME/CFS (from within the quantitative cohort or Patient Advisory Group) and staff or professionals linked to the study sites. A small number of additional expert contributors (up to 10) may be included where required.

Qualitative data collection will include interviews and observations, with up to 150 hours of observation undertaken across the four delivery sites (up to 37.5 hours per site). Observations will focus on patient-clinician interactions, service delivery models, referral pathways, and systemlevel processes relevant to care for LC and ME/CFS.

Intervention Type

Other

Primary outcome(s)

1. The development of a national service framework (NSF) for Long COVID and ME/CFS. measured using The primary outcome measures that will be used in different work packages are WP1: DPROMs including; Yorkshire Rehabilitation Scale (YRS), DSQ-SF and FUNCAP27 to capture symptom burden as well as HERITAGE general health questionnaire to capture demographic and diagnosis information. WP2: Health-related quality of life (EQ-5D-5L) to calculate QALYs and service utilisation as well as a health economic questionnaire. WP3: Qualitative study. Interviews, observations and formation of the Quality Improvement Collaboration. at For WP1&2: Baseline, follow-ups at 3, 6, 9 and 12 months. For WP3: Participants invited for interviews will take part in one interview only, lasting up to 60 minutes. Interviews may be split into shorter sessions if preferred. The QIC will run at 6-weekly intervals (two hours per session) during the course of the project. Members will be invited to commit to attending sessions regularly to support relationship-building and coherence. However, there will be flexibility around attendance and members can attend as many or as few sessions as they wish. Ethnographic observations: Research staff from the university of Leicester will be based at sites for full/half days and/or

attending for a week at a time (37.5 hours in total for each of the four sites) observing where consent is received by all parties. Up to 150 hours of observations will be undertaken.

Key secondary outcome(s)

1. Symptom burden and functional impact in participants with Long Covid and/or ME/CFS measured using condition-specific patient-reported outcome measures, including the Yorkshire Rehabilitation Scale (YRS), DePaul Symptom Questionnaire – Short Form (DSQ SF), and FUNCAP27, at baseline and 3, 6, 9 and 12 months

2. Health-related quality of life measured using the EQ 5D 5L questionnaire to calculate quality adjusted life years (QALYs) at baseline and at 3, 6, 9 and 12 months

1. Diagnostic overlap between Long Covid and ME/CFS is assessed using participant-reported diagnostic information collected via the HERITAGE general health questionnaire at baseline and at 3, 6, 9 and 12 months

2. Healthcare utilisation and health and social care costs are measured using a bespoke health economics questionnaire and linked routine service use data at baseline and at 3, 6, 9 and 12 months

3. Vocational outcomes, including employment status, working hours, and return to work status, are measured using participant self-report questionnaires at baseline and at 3, 6, 9 and 12 months

4. Patient experience, equity of access, and quality of care are explored through qualitative interviews, ethnographic observations, and outputs from the Quality Improvement Collaborative (QIC), conducted once per participant for interviews and longitudinally across the study period for observations and QIC activities

Completion date

31/12/2028

Eligibility

Key inclusion criteria

Inclusion criteria for WP1 and WP2:

1. Aged 18 years and over
2. All genders
3. Ability to provide informed consent
4. Have had symptoms of persistent LC or ME/CFS for >2 years

Clinic cohort:

1. Individuals who at study baseline, have received, are currently receiving or are about to receive (i.e., known appointment date within <3 months) specialist LC/ME/CFS services at one of the four participating NHS sites ('HERITAGE clinics' refers to existing NHS services and not researchspecific clinics).

2. Individuals who are initially part of the non-clinic cohort (defined below) and who receive specialist services from HERITAGE clinics during study follow-up and have at least 3 months of follow-up data after service receipt.

Non-clinic cohort:

1. No history of receiving specialist services for LC or ME/CFS from HERITAGE or non-HERITAGE clinics in the last 3 years.
2. GP diagnosis of LC or ME/CFS or subjective report of LC or ME/CFS, or selfreported LC or ME

/CFS symptoms without requiring a confirmed diagnosis at enrolment. Any diagnostic assessment undertaken during followup forms part of routine NHS care and is not conducted as part of this study.

During study follow-up:

1. Those who receive specialist service (including diagnosis) from HERITAGE clinics will join the clinic cohort, provided that they have at least 3 months of follow-up data after service receipt.
2. Those who receive specialist service (including diagnosis) from non-HERITAGE clinics will be excluded from further follow-up.
3. Those with subjective report of LC or ME/CFS who subsequently receive an alternative diagnosis to LC or ME/CFS will be excluded from further follow-up.
4. Those with subjective report of LC or ME/CFS who do not receive GP or specialist diagnosis during study follow-up (due to delays in the diagnostic pathway) will be followed up until study completion. Their data will be excluded from base case analysis but included in sensitivity analyses.

Inclusion criteria for WP3:

1. Aged 18 years and over
2. All genders
3. Ability to provide informed consent
4. Ability to communicate in English

Clinic cohort:

1. Currently using, referred to, or recently discharged from existing NHS specialist LC/ME/CFS services at HERITAGE study sites (Leeds, Leicester, Hertfordshire, Cornwall)

Non-clinic cohort:

1. No specialist LC/ME/CFS service use in the last 3 years
2. GP diagnosis or selfreported LC/ME/CFS symptoms (no requirement to undergo diagnostic workup as part of the study)
3. Participants may join WP3 by contacting the WP3 research team directly via the study email (as advertised on the HERITAGE website and public materials)
4. Clinical diagnosis of LC and/or ME/CFS or subjective symptoms of LC and/or ME/CFS and set to receive specialist diagnostic work-up during study follow-up. Any diagnostic workup they may undergo is part of routine NHS care and is not performed for, or required by, the study.
5. For those living with LC, have had LC symptoms for >2 years (persistent LC)

Staff cohort:

1. Working within, referring to, or involved in providing, planning, or supporting LC/ME/CFS specialist services in Leeds, Leicester, Hertfordshire or Cornwall (HERITAGE Clinics)
2. Identified and approached by site Principal Investigators or Clinical Research Fellows

The Quality Improvement Collaborative (QIC) cohort:

1. People involved in providing, referring to, or receiving LC/ME/CFS specialist services at the participating NHS sites
2. May include staff, patients and carers (where relevant)

Carers:

Carers may take part in WP3 only when supporting a patient participant at the request of that patient during an interview, clinic observation or QIC activity. Carers must be aged ≥ 18 and able to provide informed consent. Carers are not independently recruited into WP1, WP2 or WP3.

Healthy volunteers allowed

Yes

Age group

Mixed

Lower age limit

18 Years

Upper age limit

100 Years

Sex

All

Total final enrolment

0

Key exclusion criteria

Exclusion criteria for WP1 and WP2:

Clinic cohort:

1. Individuals who, during followup, receive an alternative diagnosis or enter nonHERITAGE specialist services will be withdrawn from followup for WP1/WP2
2. Individuals will be excluded if they are receiving or due to receive LC/ME/CFS specialist care at an NHS service not participating in HERITAGE
3. Individuals unable to consent or aged under 18 years will be excluded

Exclusion criteria for WP3:

Participants will be excluded from WP3 if:

1. They cannot provide informed consent for qualitative activities
2. They are too unwell to take part safely or meaningfully, even with breaks and adjustments

WP3 non-clinic cohort – exclusion criteria:

Participants will be excluded from WP3 if:

1. They cannot provide informed consent for qualitative participation
2. They are unable to participate safely or meaningfully in an interview, even with reasonable adjustments
3. English language communication is insufficient for qualitative data collection

Carers (WP3 only) – exclusion criteria:

1. Carers may be involved only when supporting a WP3 participant (patient) during:
 - 1.1. Interviews
 - 1.2. Clinic observations, or
 - 1.3. QIC meetings
2. Carers will be excluded if:
 - 2.1. They are aged under 18 years
 - 2.2. They cannot provide informed consent
 - 2.3. Their participation would introduce safeguarding concerns, or
 - 2.4. They are unable to participate safely or meaningfully in the activity

2.5. Carers are not independently recruited into WP1, WP2 or WP3 and do not have clinical inclusion/exclusion criteria beyond the above

Staff (WP3) exclusion criteria:

Staff participants will be excluded if:

1. They do not work in, refer to, or support specialist LC/ME/CFS services at participating HERITAGE NHS sites
2. Their employing NHS organisation does not grant permission for participation
3. Individuals will be excluded from QIC participation if they do not work within, receive care from, or provide support to LC/ME/CFS specialist services at participating HERITAGE NHS sites
4. Individuals will be excluded from QIC participation, if they are unable to participate safely or meaningfully in QIC meetings
5. Individuals will be excluded from QIC participation, if they are unable to attend the scheduled QIC sessions

Exclusion criteria for all work packages:

1. Individuals under 18 years of age
2. Individuals unable to provide informed consent
3. Individuals who do not have experience of Long Covid (LC) or ME/CFS healthcare needs and therefore do not meet study aims
4. Individuals for whom participation is deemed inappropriate due to safeguarding or clinical concerns, based on advice from their GP or usual clinical team

Date of first enrolment

01/05/2026

Date of final enrolment

31/12/2028

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University Hospitals of Leicester NHS Trust

Leicester Royal Infirmary

Infirmary Square

Leicester

England

LE1 5WW

Study participating centre

Hertfordshire Community NHS Trust

Unit 1a Howard Court

14 Tewin Road
Welwyn Garden City
England
AL7 1BW

Study participating centre

Royal Cornwall Hospitals & West Cornwall Hospital Laboratory

Royal Cornwall Hospitals NHS Trust
Treliske Hospital
Treliske
Truro
England
TR1 3LJ

Study participating centre

Leeds Community Healthcare NHS Trust

3 White Rose Office Park
Millshaw Park Lane
Leeds
England
LS11 0DL

Sponsor information

Organisation

University of Leeds

ROR

<https://ror.org/024mrxd33>

Funder(s)

Funder type

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan**IPD sharing plan summary**

Not expected to be made available