ISRCTN12242529 https://doi.org/10.1186/ISRCTN12242529

# How common is late-onset Pompe disease and limb girdle muscular dystrophy 2a in children and young people and adults treated for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): A cross-sectional study.

**Submission date**
17/02/2023

**Recruitment status**
No longer recruiting

**Registration date**
24/04/2023

**Overall study status**
Completed

**Last Edited**
10/09/2025

**Condition category**
Nervous System Diseases

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

## Plain English summary of protocol

Background and study aims
Myalgic Encephalomyelitis or Chronic Fatigue Syndrome (ME/CFS) is relatively common in adults and children and young people (CYP). To receive a diagnosis, CYP and adults must have: debilitating fatigue made worse by activity, worsening symptoms after activity, and sleep problems. Those with ME/CFS are disabled and use significant health care resources over a considerable period prior to accessing ME/CFS treatment.

Pompe disease (also named glycogen storage disease type II, acid maltase deficiency, OMIM #232300) is a rare metabolic myopathy caused by a deficiency of alpha-glucosidase. This results in the intra-lysosomal accumulation of glycogen. Fatigue is common in those with late-onset Pompe disease. It affects over 66% of those with the condition and is the presenting symptom in 25% of patients.

Limb girdle muscular dystrophy 2A (LGMD2A) also known as Calpainopathy is an autosomal recessive form of limb girdle muscular dystrophy. It is caused by mutations in the calpain 3 gene which gives instructions to produce a protein important to the muscle fibres. The age of onset of muscle weakness is extremely variable; the most common being between 8 and 15 years. Common symptoms include fatigue.

Many of the symptoms used to make a clinical diagnosis for ME/CFS overlap with the symptoms experienced by patients with Pompe disease or LGMD2A. Anecdotal reports suggest that some patients with Pompe disease have been treated in ME/CFS clinics for many years before the correct diagnosis is made. These patients are unlikely to get better with ME/CFS treatment approaches. A diagnosis of Pompe disease is important as it enables access to treatment that improves quality of life and life expectancy. A diagnosis of LFMD2A also enables patients to access appropriate supportive treatment.

Who can participate?
Patients aged 8 - 70 years with ME/CFS who live in the UK.

What does the study involve?
Participants are asked to complete one questionnaire and provide a saliva sample via an Oragene kit

What are the possible benefits and risks of participating?
You may need to spend some time talking to a research nurse so we can understand if you are interested in the study. You will need to arrange a time to talk on the phone to a research nurse about the study. This will take about 45 minutes. If you take part, you will have to spend some time completing the online questionnaire and providing the saliva sample. The questionnaire will take you about 20 minutes to complete and the saliva sample will only take minutes to do. The main disadvantage is if you receive an unclear result from the genetic testing. If this happens, you might have Pompe disease or LGMD2A and you may be asked to provide another sample. Support from the research team will be given, and you will be offered a referral to a local genetic service in the NHS. You may also feel a bit worried whilst you wait for your result. However, support from the research team and Association for Glycogen Storage Disease-UK (a charity) and will be available to you if you need it. To remind you, the wait for results will be up to 6-months. However, there are benefits to taking part. The main benefit is finding out whether you have Pompe disease or LGMD2A and this will help you get the most effective type of treatment. You may learn something about how a research trial works. Some people with ME /CFS like to know that they are helping others with ME/CFS in the future

Where is the study run from?
University of Bristol (UK)

When is the study starting and how long is it expected to run for?
April 2022 to September 2025

Who is funding the study?
Sanofi (France)

Who is the main contact?
If you are interested in finding out more, please click on this URL: https://redcap.link /GEMinterest.
You will find our online information sheets and an optional form to leave your contact details. If you do decide to leave your contact details, we will ask you a few questions to see if you're eligible to take part in the study. Thank you.

# Contact information

### Type(s)
Scientific

### Contact name
Ms Georgia Treneman-Evans

### Contact details
The Centre for Academic Child Health (CACH)
Bristol Medical School

Canynge Hall
39 Whatley Road
Bristol
United Kingdom
BS8 2PS
+44 117 4554503
georgia.treneman-evans@bristol.ac.uk

# Additional identifiers

### Integrated Research Application System (IRAS)
313068

### Central Portfolio Management System (CPMS)
54805

### Protocol serial number
SGZ-2020-13038

# Study information

### Scientific Title
GEM Study: Prevalence of genetic diseases in ME/CFS patients

### Acronym
GEM

### Study objectives
A proportion of adults and children and young people who are given a diagnosis of ME/CFS have undiagnosed Pompe disease or LGMD2A which explains their clinical symptoms

### Ethics approval required
Ethics approval required

### Ethics approval(s)
Approved 28/07/2022, HRA and Health and Care Research Wales (HCRW) (HRA RES Centre Manchester 3rd Floor Barlow House 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; -; HCRW.approvals@wales.nhs.uk), ref: 313068

### Primary study design
Observational

### Study design
Observational cross-sectional

### Study type(s)
Screening

### Health condition(s) or problem(s) studied
Myalgic Encephalomyelitis or Chronic Fatigue Syndrome (ME/CFS)

## Interventions

Current interventions as fo 03/05/2024:

All data will be collected via REDCap, which is an online secure and safe platform. Participants will complete online forms to provide the following:
1. Consent to the study
2. Personal details such as gender and ethnicity
3. Symptom data, including fatigue severity
4. Quality of life data
5. Pain data
6. Well-being data

_____

Previous interventions:

Data collection:
Data collection using REDCap: The Paediatric service uses online systems to collect assessment and outcome data online in CYP. The research team at the service have developed, tested and use online consent to enable participants to take part in trials. Therefore, all participants will use REDCap to record their answers. Only members of the research team will have access to the participant's data recorded in REDCap.

Demographic Data: we will collect the following demographic data: date of birth, gender, ethnicity, NHS number.
Symptom data: We will collect the following data at assessment (yes=frequently present): cognitive problems, headaches, muscle aches, joint aches, sore throats, tender lymph nodes, nausea, dizziness, palpitations, respiratory problems.
Patient Reported Outcome Measures (PROMs): We will collect the following Patient Reported Outcomes Measures which are routinely collected at assessment in the ME/CFS clinics: Fatigue (Chalder fatigue scale, 11 items; Physical Function (SF-36 physical function subscale); pain (visual analogue scale); Anxiety and Depression (Adults: Hospital Anxiety and Depression Scale, Children and young people: Revised Childrens Anxiety and Depression Scale).
At Royal United Hospital Bath, demographic data and the PROMs are collected using REDCap and we will therefore obtain consent to use this data, rather than ask the CYP to complete these questionnaires again. We will therefore only collect symptom data on REDCap for CYP. At North Bristol Trust, participants will be asked to provide all the data using REDCap.
Sample collection: Saliva samples will be collected from all consenting participants. They will be labelled with barcode ID numbers and personal information will not be passed to researchers /technicians processing or analysing the samples. Participants can choose to collect saliva at home or in clinic. If participants chose to collect saliva at home, we would send them an Oragene Saliva collection kits with a returned address envelope, sample pot and instructions.
The instructions include a link to a video describing how to collect the saliva. Previous feasibility work has demonstrated that adults with ME/CFS have found these easy to use at home and have produced saliva from which good quality DNA can be extracted. If participants prefer, samples can be collected in the specialist ME/CFS service with help from the research nurse (or the recruiting clinician). All samples will be posted to the Bristol Bioresource Laboratories (BBL), Oakfield House, University of Bristol. If there is indication of Pompe disease and/or LGMD2A, these participants will undergo further testing to confirm the diagnosis of Pompe disease /LGMD2A. This is likely to include providing a second saliva sample for testing or a blood sample for DBS testing in a certified NHS clinical setting.

### Intervention Type
Other

### Primary outcome(s)
1. Symptoms are measured via a 4-point Likert scale from 1 (all of the time) to 4 (none of the time) at baseline.
2. Fatigue is measured by the Chalder Fatigue Questionnaire which is 11 items. Participants answer these items on a 4-point Likert scale from 1 (less than usual) to 4 (much more than usual) at baseline.
3. Pain is measured using a visual analogue scale (VAS) at baseline.
4. Anxiety and depression for adults is measured by the Hospital Anxiety and Depression Scale which is 14 items. Participants answer these items on a 4-point Likert scale at baseline.
5. Anxiety and depression for children and young people is measured by the Revised Children's Anxiety and Depression Scale which is 47 items. Participants answer these items on a 4-point Likert scale from 1 (never) to 4 (always) at baseline.

### Key secondary outcome(s)
There are no secondary outcome measures

### Completion date
01/09/2025

## Eligibility

### Key inclusion criteria
1. Adults Inclusion: aged 18-70 years with a diagnosis of ME/CFS
2. CYP Inclusion: aged 8-17 years with a diagnosis of ME/CFS
3. Individuals who live in the UK

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
8 Years

### Upper age limit
70 Years

### Sex
All

### Total final enrolment
543

### Key exclusion criteria
Recovered or unable to provide informed consent

### Date of first enrolment
01/09/2022

### Date of final enrolment
31/08/2024

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**Royal United Hospitals Bath NHS Foundation Trust**
Combe Park
Bath
United Kingdom
BA1 3NG

### Study participating centre
**North Bristol NHS Trust**
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

## Sponsor information

### Organisation
University of Bristol

### ROR
https://ror.org/0524sp257

## Funder(s)

### Funder type
Industry

### Funder Name
Sanofi

### Alternative Name(s)
sanofi-aventis, Sanofi US, Sanofi-Aventis U.S. LLC, Sanofi U.S.

### Funding Body Type
Government organisation

### Funding Body Subtype
For-profit companies (industry)

### Location
United States of America

## Results and Publications

### Individual participant data (IPD) sharing plan
The data will be anonymised and available from https://data-bris.acrc.bris.ac.uk/. It will be posted on there within 3-months of recruitment finishing. Other researchers will be able to access the data for 2-years after the study has stopped. We will not keep the study data open access longer than this as we do not currently have funding for long term storage and we consider that 2-years is sufficient time for other researchers to use the data.

### IPD sharing plan summary
Data sharing statement to be made available at a later date

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version 3 | 10/01/2023 | 30/03/2023 | No | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |