The GEM Study: GEnetic Diseases in ME/CFS Patients.

How common are two genetic diseases in children, young people and adults treated for Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS)?

Information Leaflet for Young People Aged 11-15 Years.

We would like to invite you to take part in a research study which will tell us whether late-onset Pompe disease or Limb Girdle Muscular Dystrophy 2A is found in young people and adults with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.

Before you decide whether you would like to take part, it is important for you to understand why the study is being done and what it will involve. The leaflet is divided into two parts.

- Part 1 briefly tells you about the study and what will happen if you choose to take part.
- Part 2 (page 3) gives further details about how the study will be run.

Please read this leaflet carefully. You can talk about it with your family, friends, doctor, or us. Ask us if there is anything you don't understand or if you want more information. Take the time to decide whether or not you want to take part. **Thank you**.

Part 1

Why are we doing this study?

Pompe disease (also named glycogen storage disease type II or acid maltase deficiency) is a rare genetic condition caused by a fault or spelling error in the GAA gene. It causes a harmful build-up of complex sugars in the body's tissues.

Limb Girdle Muscular Dystrophy 2A (LGMD2A) also known as Calpainopathy is also a genetic condition. LGMD2A is caused by faults or spelling errors in the Calpain-3 gene which gives instructions to produce a protein important to the muscle fibres.

If you'd like to find out more about Pompe disease and LGMD2A, **please scan the QR code at the bottom**.

Long-lasting tiredness is common in those with Pompe disease and LGMD2A and it impacts most of those with the condition. Many of the symptoms used to make a ME/CFS diagnosis overlap with the symptoms experienced by people with Pompe disease or LGMD2A. It is therefore possible that people with Pompe disease or LGMD2A may come to ME/CFS clinics with the main symptom of long-lasting tiredness. Informal reports suggest that some people with Pompe disease have been treated in ME/CFS clinics for many years before the correct diagnosis is made.

If people with Pompe disease or LGMD2A are currently being treated in ME/CFS clinics, we need to find a way to identify these people and **offer effective treatment**.
We want to know if people with Pompe disease or LGMD2A are being treated for ME/CFS in either an adult or young person specialist ME/CFS clinic.

Why have I been asked to take part?

You have been asked to take part in this study because you are aged between 11 and 15 years and have a diagnosis of ME/CFS.

Do I have to take part?

You do not have to take part in this study. If you want to speak to the research team, they will explain more about the study, but this will not commit you to taking part.

If I agree to take part, can I change my mind?

Yes. You can leave the study at any point and, if you would like us to, we will take out some of the information we collected about you at any point before we look closely at the data.

Leaving the study at any time will not affect the standard of medical care you will receive.

What will I be asked to do if I take part?

First step:

1. If you would like to hear more about the study, a member of the research team will arrange a time to talk to you over the telephone. They will explain the study to you and your parents/carers, and answer any questions you may have. They might ask you about how you are you feeling about the study to make sure you are happy to take part.

1. If you want to take part in the study, you will be asked to fill in an online form to show us that you agree to take part in the study. Your parent/carer will also need to fill out a similar online form.

Second step:

2. Once you have agreed to take part and you as well as your parent/carer have completed the online forms, you will be asked to complete some online questions about you and how you're feeling. These questions won't take long to complete.

2. To find out whether Pompe disease or LGMD2A is found in young people and adults with ME/CFS, we will collect a saliva sample from each person who takes part in the study. A member of the research team will send an **Oragene saliva collection kit** to your home address for you to complete. The kit will include a returned address envelope, a sample pot, and instructions. The instructions include a link to a video describing how to collect the saliva. People have previously found these kits easy to use at home. Samples can also be collected in the specialist ME/CFS clinic with help from a nurse.

Part 2

If you are still interested in taking part in this study, please read the information below before making your decision. **We suggest that you read Part 2 with a parent/carer**.

What will happen to my saliva sample?

Your saliva sample will be used to obtain DNA at a laboratory within the University of Bristol. Some of your DNA sample will then be sent to Newcastle University for genetic testing. The laboratory in Newcastle will be looking at the spelling of the genes that are linked to Pompe disease and LGMD2A. You will be informed of the results of the genetic tests as soon as possible by a member of the research team but this may take up to 6-months. If our results suggest that you might have either Pompe disease or LGMD2A, a NHS laboratory will need to confirm this with a new sample. Your GP will be informed about the study and your genetic testing outcome.

The genetic tests will be carried out in a research setting. The results may show there are spelling differences in the genes we are looking at. These may have an unknown clinical meaning. This is why more tests may need to be done at a NHS clinical laboratory.

What will happen to my DNA sample?

If you're happy to, any DNA remaining after testing will be stored at the University of Bristol for future genetics research. Your sample may be made available to researchers working in universities, hospitals or other organisations in the UK or abroad. We may ask for a fee from researchers to help cover the costs associated with sending them to other places. We will **not** sell or make any profit from the samples you donate, and they will only be used in ethically approved research. Others will not be able to identify you from the sample.

Are there any disadvantages to taking part in the study?

You may need to spend some time talking to a member of the research team so we can understand if you are interested in the study. You and your parents/carers will need to arrange a time to talk on the phone to them about the study.

If you take part, you will have to spend some time completing the online questionnaires and providing the saliva sample. The questionnaires will take you about 20 minutes to complete and the saliva sample will only take minutes to do. Your parent/carer may need to help you.

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) will be available to you if you need it. To remind you, the wait for results will be up to 6-months.

Will I experience any side effects from taking part in this study?

No. There are no known risks from completing the questionnaires or a saliva sample.

What are the benefits from taking part in this study?

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 young people with ME/CFS like to know that they are helping others with ME/CFS in the future.

What will happen when the study stops?

Your participation in the study will not change the NHS care you receive. Once you completed the questionnaires and provided enough DNA, you will continue to receive NHS care. After the study stops and you want to know the study results, let us know and we can send them to you.

Assent and consent

We have to be completely certain that you are happy to join this study, so we will ask you to sign an assent form (i.e., to show your agreement to take part in the study). Once you have signed the form, you will still be free to leave the study at any point. Just tell us if this is the case. Whether or not you wish to take part, you will continue to receive the same care from the NHS team.

How will we use information about you?

We may need to use information from your medical records for this research project. This information will include your NHS number, name, date of birth, gender, ethnicity, and routine clinical data. People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you **safe and secure**. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you tell us something that makes us worried about your safety or the safety of those around you, we may have to discuss this with somebody else. This means that what you say would not be kept completely private if we were concerned about you or those around you. We would do the same if you told us something in clinic.

You can find out more about how we use your information by asking someone from the research team, sending an email to data-protection@bristol.ac.uk or calling the University Data Protection Officer on 0117 3941824.

What will happen if I feel unwell during the study?

If during the study you start to feel unwell (e.g., if you feel anxious or depressed, or if you have a fever), you should speak to your parents/carers and contact your local care providers (e.g., your GP or paediatrician). The research team provide specialist treatment for ME/CFS but cannot provide treatment for other problems you may have.

If you do contact the research team about other concerns (e.g., feeling anxious or depressed), the research team will do their best to help. If they feel it's appropriate, they may pass the information on to your local care providers and try to inform you of other services which may help you. The research team may not be able to reply to your queries straight away. This is why you should always speak to your parents/carers and contact your GP if you have any concerns.

Does everybody involved in the study have the right police checks?

Yes. Those who are working with people within the study have had police checks to make sure they are safe to work with children and adults.

What will happen to the results of the study?

This study will give us information on whether Pompe disease or LGMD2A is found in young people and adults with ME/CFS. We will share the results of the study to help people in the future get the best possible treatment for their condition.

Who is organising and financially supporting the study?

This research is organised by Dr Katy Pike and the team at the University of Bristol.

The study is funded by Sanofi and is sponsored by the University of Bristol.

What should I do if I have a problem with the study?

If you have any problems with this study, please speak to your parents/carers, Dr Katy Pike, or any member of the clinical team that you know. Dr Pike's contact information can be found below. You can also talk to the NHS in the usual way via the Patient Advice and Liaison Services (PALS) on 01225 825656.

Ethical approval

Ethical approval means that we have received a favourable opinion from the NHS Research Ethics Committee. An independent group of people reviewed our study and agreed it was ethical.

Who can I contact for further information?

Research Lead: Dr Katy Pike.

ruh.tr-CFSResearch@nhs.net

Please click here or scan the QR code to **find out more** on DNA testing and storage: