Participant Information Sheet for FH Index Patients

* Family studies of patients with Familial Hypercholesterolaemia (FH)

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. Part 1 tells you the purpose of the study and what will happen if you take part. Part 2 gives you more detailed information about the conduct of the study. Please take time to decide whether or not you wish to take part.

Thank you for reading this.

Part One

What is Familial Hyercholesterolaemia (FH)?

FH is an inherited condition which results in high cholesterol levels in the blood. 'Familial' means it is inherited through families. 'Hypercholesterolaemia' is the medical term for high blood cholesterol – 'hyper' means ***raised*** and 'aemia' means ***in the blood***. It can cause the arteries to narrow and clog and can lead to early angina and heart attacks (coronary heart disease). However, there are effective treatments available and, combined with a healthy diet and lifestyle, people with FH can expect to live a normal and healthy life.

FH is caused by an alteration in a single gene. It is inherited in such a way that immediate blood relatives of individuals with FH (parents, brothers, sisters, children) have a 50:50 chance of also having FH.

How is FH diagnosed?

A diagnosis is based on a combination of high cholesterol levels, clinical signs, family history and genetic (DNA) testing. DNA testing can be helpful to confirm the diagnosis of FH. If a recognised DNA alteration is found in one of the 3 genes known to cause FH, this confirms the diagnosis of FH. It also allows the testing of family members to see if they too have inherited the same DNA alteration. However, sometimes a DNA alteration is found and it is not clear whether it causing FH or whether it is an incidental finding that does not cause FH. Such DNA alterations are called 'variants of uncertain significance' (VUS) or 'unclassified variants' (UVs). This means that the family member may indeed have an inherited form of high cholesterol but this DNA test cannot be used to diagnose other members of the family.

* This is a working title. The scientific protocol title is: Variants of Uncertain Significance in Familial Hypercholesterolaemia. Can family cosegregation analysis help determine pathogenicity?

What is the purpose of the study?

The purpose of this study is to gather evidence about the VUS's that we have identified in FH patients to help decide whether or not they cause FH. The study will involve family testing of relatives of FH patients in whom we have identified a VUS. This will involve both DNA testing and cholesterol testing on a blood sample. Information from family testing of cholesterol and DNA testing will be compared to give us more evidence about the clinical significance this genetic result. In your family, the researchers will investigate whether or not the VUS is causing FH.

Why have I been chosen?

You have been asked to take part because you have had a genetic test for FH and the laboratory identified a VUS. This is an uncertain genetic diagnosis and due to this uncertainty, your family members have not been offered genetic testing as part of the normal FH Family Testing Service.

Do I have to take part?

Taking part in the study is voluntary and it is up to you to decide whether to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign and return the consent form (consent to be contacted) enclosed. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen if I take part?

Once you have returned your completed consent form, you will be contacted by a member of the FH clinical team. The study will be discussed with you and you will have the opportunity to ask questions. If you decide to participate, you will be asked to provide us with details of your family members, so they can be sent letters inviting them to participate in this study. Alternatively, we can give you the invitation letters and you can give these to your family members yourself.

What will happen to my family members if they take part?

They will receive a letter and if they consent, they will be contacted by a member of the Wales FH Cascade Testing Service. They will be offered a clinic appointment with a member of the FH clinical team to discuss family testing. If they decide to participate, they will be asked to provide a small (10mL) blood sample. This will be used to measure cholesterol levels and enable genetic testing to be carried out to identify if they carry the same VUS as you. If their cholesterol levels are raised, they will be advised to get a referral to their local lipid clinic and we will be able to help organise this.

What are the possible disadvantages of taking part?

If the research study does not provide enough evidence to give clarity on the clinical significance of the VUS then this may be disappointing for yourself and your family members who participated.

Your family member's cholesterol levels will be measured and if found to be raised this may cause them some anxiety. However, this can be seen as a benefit. If it is appropriate, they will be offered a referral to a lipid clinic. The lipid clinic specialist will make a full assessment of FH and may make a diagnosis. This is a treatable condition and evidence has shown that the earlier FH is diagnosed and treated, the lower the risk of early heart disease.

What are the possible benefits of taking part?

If the family study provides enough evidence, then the clinical significance of the VUS may become known and will be communicated to you. If the VUS is found to be FH-causing, then the rest of your family members (who didn't take part in the research) can be offered genetic testing to see if they have inherited the condition.

If the VUS is proven not to be FH causing you will be advised of this and it will be clear that this variant should be regarded as being an incidental variant of no significance, and that any family testing should be carried out using cholesterol levels alone. The information would clarify this point for your family.

What will happen if I don't want to carry on or if there is a problem?

You are free to withdraw from the study at any time without it affecting your future care. Any complaint about the way you have been dealt with during the study will be addressed. More details on this can be found in Part 2.

This completes Part 1 of the information sheet. If the information in Part 1 has interested you and you are considering taking part, please continue to read the following information in Part 2 before making any decision.

Part 2

Will my taking part in this study be kept confidential?

All patient information will be kept confidential within the All Wales FH Service, in line with the NHS confidentiality guidelines. Any published data will be anonymised in accordance with the Data Protection Act 1998. Only authorised persons will have access to identifiable data. These persons include specific NHS staff (or Cardiff University staff with an honorary NHS contract). These include members of the All Wales FH Cascade Testing Service and specific members of the genetic testing laboratory who carry out the testing of FH

Data will be kept on a secure NHS database specific for FH families and will be kept for as long as this database is maintained for the purpose of coordinating this research and the Wales FH service. This is important for this type of study because as more evidence becomes available for specific VUS's, then the clinical significance may change. This may have implications for testing of other family members. In such a case, the researcher/a member of the FH Cascade Testing Service will attempt to re-contact the research participant and will communicate this new clinical significance.

Involvement of the General Practitioner (GP)

If you consent to this, your GP will be notified if you decide to take part in this study and your cholesterol results will be communicated to him/her.

What will happen if I don't want to continue with the study?

If you withdraw from the study and do not wish for any of your relatives to be tested, then the family testing in your family will stop. If you withdraw, but are happy for the family testing to continue, but you do not wish to know the outcome of the family testing and whether this resulted in gathering enough evidence to say whether your VUS is FH-causing, then this is also possible.

What if there is a problem?

If you have a concern about any aspect of the study, you should ask to speak with the researcher who will do their best to answer your questions (Tel: 02920 743864). If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, please contact Mr Chris Shaw, Research Governance Co-ordinator at the Research and Commercial Division, Cardiff University, 7th Floor, 30-36 Newport Road, Cardiff, CF24 0DE, 02920875834

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against Cardiff University or Cardiff and Vale University Health Board but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

What will happen to the results of the research study?

The results of the study will allow the development of the Wales FH Cascade Testing Service and improve the clinical utilization of FH genetic testing results. They may also be published in a relevant scientific journal.

Who is organising and funding the research?

The researcher is employed by Wales Gene Park (part of Cardiff University). The clinical elements of the study will be funded by the All Wales FH Cascade Testing Service.

Who has reviewed the study?

This study has been reviewed and approved by Cardiff and Vale University Health Board R&D and the Research Ethics Committee for Wales.

Contact Details

If there is anything that is not clear or you would simply like more information please contact the researcher using the following contact details:

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