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Participant information sheet

Patients with stored samples

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A study to assess how common Cholesteryl Ester Storage Disorder (CESD) is in patients with clinical features of Familial Hypercholesterolemia (FH)

We would like to invite you to take part in our research study. Before you decide, please read the information below which explains why the research is being done and what it would involve for you.

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.

Talk to others about the study if you wish. You may also speak to a member of the research team who will go through the information sheet with you and answer any questions you may have. Contact details of the research team are given at the end of this document.

Glossary of terms used in this information sheet	
FH	Familial Hypercholesterolemia is a condition which runs in families and leads to raised levels of cholesterol that increase the risk of early onset heart disease.
CESD	Cholesteryl Ester Storage Disorder is a condition that has some features similar to FH.
DNA	DNA is short for *deoxyribonucleic acid* which contains the code that gives instructions for how cells in our body grow and function.
Genetic Variants	These arise from changes in the DNA code. This could be thought of as spelling mistakes in the genetic code. The effect of these spelling mistakes can be benign e.g. affecting eye colour or may affect health e.g. causing raised blood cholesterol.
Negative genetic result	We can test a patient's DNA for common genetic variants that are known to cause raised blood cholesterol. Patients are informed that they have had a negative genetic result if their DNA does not have any of the common variants that we routinely test for.
Index patient	The index patient is the first member of a family that is identified as having clinical features of FH.

Part 1

What is the purpose of this study?

Familial Hypercholesterolemia (FH) is an inherited condition that causes high blood cholesterol levels and increases the risk of coronary heart disease. FH can be effectively treated with cholesterol lowering tablets such as statins. The All Wales FH Service tests patients' DNA for genetic alterations that can cause FH. When a genetic diagnosis of FH is made, relatives of this 'index' patient can also be offered a DNA test for FH on a sample of blood or saliva. In Wales over 1000 people have been offered testing for FH genes over the last 3 years. In approximately one third a genetic variant has been found in one of the common FH genes. In the remaining two thirds a genetic variant has not been detected. This does not mean that these individuals do not have a genetic cause of their high cholesterol. It may mean that the relevant genes have not been tested yet.

Recently, a condition known as Cholesteryl Ester Storage Disorder (CESD) has been shown to be caused by a DNA alteration in a gene that changes the way cholesterol is processed by the body. There are severe and mild forms of CESD. The milder form can have features that are very similar to classical FH. It is also a cause of early onset coronary heart disease and can be treated. It is possible that some index patients with clinical features of FH may have this genetic alteration. Therefore we would like to offer this test to patients who have been tested for FH but for whom a genetic variant has not been found as yet.

When patients' genes are tested for FH the leftover DNA is stored in case new genetic variants that cause FH are found in the future. We would like to test stored DNA from patients who have previously had a gene negative result to find out if they have a CESD genetic variant.

Why have I been invited to take part?

You have been invited to take part because you have been tested as part of the All Wales FH Service and have had a "negative" genetic result for FH (that is no genetic variants have been found yet for you).

Do I have to take part?

No. It is up to you whether you want your sample to be included or not. If you decide to take part, you should keep this information sheet and you will be asked to sign a consent form. You can withdraw from the study up until the time the sample is analysed. Your medical treatment will continue as before.

What will happen if I do decide to participate?

Once the consent form has been signed and returned to the study team most people will not have to do anything further. Some people will be contacted by the study team if there is not enough of their DNA left in storage to perform the test. A kit for collecting a mouthwash sample will be sent through the post with instructions on how to take the sample and where to return it by post. Most saliva samples are adequate for this purpose so there should be no need to have a further blood sample taken. If however, the mouth wash sample does not yield enough DNA to do the test then you may be asked if you wish to provide a blood sample for this purpose

Expenses and payments

You should not incur any expenses to take part in this study, therefore no payments will be made for expenses.

What are the possible disadvantages and risks of taking part?

Patients should not experience any physical discomfort or harm. If there is not sufficient sample stored then a mouthwash sample will be used to allow the laboratory to retrieve some DNA for the test. This should avoid the potential inconvenience and discomfort of giving a blood sample. It is unlikely that a further blood sample will be required.

Some patients may be found to have the CESD genetic variant. If the CESD variant is found then patients will be invited to discuss the implications of this with their lipid care team and to have their medication reviewed accordingly.

Are there any possible benefits to taking part?

Patients may be found to have the CESD genetic variant. This means that their medication will be reviewed by their lipid care specialist and the implications of having the CESD genetic variant will be discussed. Patients will be invited to participate in family studies with a view to finding out if other family members also have this genetic alteration and whether they also have raised blood cholesterol levels.

If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART 2

Will my taking part in the study be kept confidential?

Yes, all patient information will be kept confidential within the All Wales FH Service, in line with the NHS confidentiality guidelines. Only authorised persons will have access to identifiable data. These persons will include NHS staff and Cardiff University Staff with Honorary NHS contracts or Research Passports permitting them to access patient data for this project. These include members of the All Wales FH Service and specific members of the genetic testing laboratories. 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 project and the Wales FH service. Any data held on Cardiff University computers will be coded using unique study identifiers rather than names and will be password protected.

Involvement of the General Practitioner (GP)

Your GP will only be notified of your participation in this study if you request this.

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

If you decide at a later date that you do not want to continue with the study you should let the study investigator know. If your test has not yet been done, this will be stopped. You may choose not to receive the result of the genetic test.

If you have the CESD genetic variant than you will be offered the opportunity for your relatives to be tested for this variant, but this is not compulsory. You and they can decide whether to take up this offer.

What if there is a problem?

If you have a concern about any aspect of the study, you should ask to speak with the researchers who will do their best to answer your questions (Tel: 029 2074 3864).

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, in the first instance 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, 029 2087 5834, shawc3@cardiff.ac.uk

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 help the development of the All Wales FH Service and improve the clinical understanding of the genetic causes of FH. The results may also be published in the scientific literature.

Who is organising and funding this research?

The investigators are Dr Ian McDowell and Dr Pauline Ashfield-Watt. They are employed by Cardiff University. Research assistance will be provided by Miss Kate Haralambos (Cardiff University). The administration associated with the All Wales FH Cascade Testing Service will be undertaken by the relevant NHS employee. Clinical care will be provided by the patient's usual clinical care team including BHF Specialist Nurses and Lipid Clinic Consultants. Genetic analyses will be subcontracted to NHS and other approved laboratories. This research is funded by Synageva Biopharma Corp.

Who has reviewed this study?

The study has been reviewed and approved by Cardiff University Research, Innovation and Enterprise Services and the National Research Ethics Service, Wales REC 3.

Contact Details

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

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