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The SOLID study Participant Information Sheet

Stratification Of LIver Disease (SOLID): **Determining the optimum biomarker strategies for the detection of advanced liver disease at the primary-secondary care interface**

Introduction

You are being invited to take part in a research study.

Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. If anything is unclear, or if you would like further information please feel free to ask the person who gave you this leaflet, or speak to a member of the research team directly on 0191 213 7208.

What is the purpose of the study?

The SOLID study aims to find out how to identify people with liver disease before irreversible damage has occurred.

People with liver disease often don't have any symptoms until the liver disease is severe, so this may not be picked up until they have cirrhosis (severe scarring of the liver). We are inviting individuals who may be at risk of liver disease to take part in the study to try to diagnose people with liver disease at an earlier stage when treatment may be more effective.

If you agree to take part, you will have a 'liver assessment' when you attend your annual routine review with your GP. This will involve blood tests to look for liver fibrosis (stiffening of the liver), which is an earlier stage of liver damage than cirrhosis (scarring of the liver). Participants will also have a liver scan (Fibroscan) to look for fibrosis. We hope to find more accurate liver fibrosis tests that could be used to help identify people with liver disease in the community.

Importantly, sometimes liver damage is reversible if it is detected early. Making lifestyle changes including losing weight, healthy eating and increasing exercise can reduce fat in the liver and reduce liver scarring. Cutting down or stopping alcohol intake also reduces liver damage. Therefore, early diagnosis of liver disease and making some lifestyle changes can prevent or slow progression to cirrhosis (severe liver damage).

In this study, we are assessing how effective the inclusion of a 'liver assessment' as part of GP health review appointments is in identifying people with undiagnosed liver disease. We will also assess how well different fibrosis tests (blood tests and the 'fibroscan' liver scan) perform in finding people with liver disease and whether they can identify people who will develop complications of liver disease in the future. **Ultimately, we hope to develop a pathway that can be routinely used to help identify people with liver disease earlier.**

Anyone identified with risk factors for liver disease will be given targeted advice to reduce their risk of developing liver disease in the future and will be offered an advice leaflet entitled "Looking after your liver – reducing your risk of fatty liver disease". Lifestyle advice addressing alcohol consumption and weight reduction, where appropriate, is usually given as part of standard care in annual primary medical reviews. People who are found to have significant liver disease during the study will receive treatment for their condition.

Why have I been chosen?

You are being asked to participate because your doctor or nurse thinks that you may be at risk of liver disease and you are already attending your GP surgery for an annual health review. Individuals with type 2 diabetes, those who are overweight or those who consume more than the recommended limits for alcohol are at risk of fatty liver disease.

Do I have to take part?

No. It is entirely up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form, and will be given this information sheet and a copy of the signed consent form to keep. If you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the clinical care you receive.

Do I have to agree to all parts of the study?

No. It is up to you to decide which, if any, of the parts of the study you are willing to participate in. If you are happy to join the study and give blood samples, but do not wish to be contacted in the future about additional studies, simply initial the appropriate boxes on the consent form and leave blank those areas that you do not wish to take part in. Additionally, if you do not want the researchers to access your medical records in the future (at 2, 5 and 10 years) to determine if you have developed any complications of liver disease then you can opt out of this part of the study.

Participation in every aspect of this study is voluntary. You may choose to take part in none, all or some of the components of the study, without your clinical care being affected in any way.

What will happen if I do not want to carry on with the study?

You are free, at any point, to decide not to carry on with the study without giving a reason, and you do not need to tell us why. You can also request to have any of your unused, identifiable samples destroyed. Existing anonymised data already collected or generated by studying samples you have already given us will be retained and used in the study.

What will happen to me if I take part?

If you agree to take part in the study, we will record some information about your health in a secure computer database. We will collect information like your age, date of birth, gender, test results (for example, blood tests or scans) and information on any other illnesses you may have or the treatment that you receive. Where possible, we will access electronic data, such as your blood test results and your treatment details, which are held on General Practice and Hospital computer systems.

You will have blood samples collected (8 teaspoonfuls of blood) so they can be analysed for a range of liver biomarkers, including FIB-4 score and ELF test, and other routine blood tests such as lipids (cholesterol) and HbA1c (a long term measure of blood sugar levels). The FIB-4 score is calculated from blood tests that are usually taken during annual review appointments. The ELF test is not currently part of routine annual medical review appointments, but is recommended by the National Institute of Health and Care Excellence (NICE) to assess liver fibrosis in people with suspected fatty liver. These blood tests will be carried out during a routine appointment if possible meaning no extra visit to the GP for the study (visit 1). You will be offered a Fibroscan to measure your liver's elasticity. It is routine practice to perform Fibroscan in people with raised FIB-4 scores or ELF tests or those who consume potentially harmful levels of alcohol. We are offering Fibroscan to all participants to see if this is more effective than using the FIB-4 score or ELF in identifying significant liver fibrosis. This Fibroscan is a painless test that uses ultrasound to measure the elasticity of the liver and determine the amount of fibrosis (scarring) in the liver. The Fibroscan will be performed at a GP practice in your practice or local practice and takes less than 5 minutes. This may require an additional visit to have the scan performed (visit 2). If the Fibroscan indicates probable significant liver fibrosis then you will be offered referral to the liver clinic for further assessment and treatment (visit 3). Appointments for the Fibroscan and assessment at the liver clinic are conducted face to face. All COVID-19 policies will be adhered to.

You will also be asked to complete a short questionnaire that will record information about your health.

As part of this study we would like to determine whether the fibrosis tests can also identify people who may develop complications of liver disease, such as liver cancer, in the future. To do this, we plan to access the electronic patient record of study participants at 2, 5 and 10 years to see if they have developed complications. Your NHS number will be used to gather this information. You are free to opt out of this part of the study if you wish.

If you agree to be contacted for future clinical studies or trials in liver disease that you may be eligible to participate in, you will be contacted to ask if you wish to receive further information. You will be under no obligation to take part in future studies, and you can ask us at any time not to be contacted further.

What will happen to my blood samples?

Some of the blood will be tested immediately for existing liver fibrosis biomarkers (FIB-4 score and ELF). The remaining samples will be stored in the Newcastle University Biobank facility or at another approved research laboratory so they can be analysed for experimental

liver biomarkers (such as ProC3 or CTX3) periodically during and after the study. These samples may be stored for months or years before analysis. The samples are stored and labelled with a code number, which links them to the information in the database without needing to know your name or anything else about you. The blood samples will be used for scientific research and may be shared with third parties including universities, academic entities and diagnostic and pharmaceutical companies, which may be based outside the UK, to undertake the analyses. Samples will be kept securely at all times in the biobank and when in transit to other laboratories.

After this study is finished and with your consent, we'd like to keep any surplus samples for use in future research studies of liver disease.

What are the possible disadvantages of taking part?

In most cases, we do not anticipate any disadvantages of taking part. Being diagnosed with liver disease could cause you worry about the diagnosis, but it does also potentially lead to you being able to have treatment to reduce your risk of progressive of liver disease if this were diagnosed. The risks of participation are very low, but having a blood sample collected can be uncomfortable for a short time or may leave a small bruise.

What the possible benefits of taking part

By taking part in the study and having the liver fibrosis assessment we may identify undiagnosed liver disease, which you can then have treatment for. We will also provide information about lifestyle changes that you can make to reduce your risk of liver fibrosis in the future. In addition, the outcome of the research could help to improve the care of other patients. You will not personally receive any financial benefit from taking part in the research.

Will my taking part in this study be kept confidential?

How will we use information about you?

The Newcastle upon Tyne Hospitals NHS Foundation Trust (NUTH) is the sponsor for this study, which is being conducted in collaboration with researchers at Newcastle University. We will be using information about you in order to undertake this study. NUTH will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly.

We will need to use information from your GP and hospital medical records for this research project.

This information will include your initials, NHS number, name and contact details. 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.

Some of your anonymised information may be sent to project collaborators in other countries. They must follow our rules about keeping your information safe.

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.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

What are your choices about how your information is used?
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.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- t www.hra.nhs.uk/information-about-patients/
- our leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to the study team nuth.nencnurses@nhs.net or the NUTH data protection officer nuth.dpo@nhs.net

As part of the study, if the liver biomarkers indicate possible significant liver fibrosis then you would be referred to the liver clinic at the Newcastle upon Tyne Hospitals NHS Foundation Trust. At this clinic a liver specialist, who may also be one of the researchers, would see you and you may be offered further tests or treatment. Relevant clinical information about diagnoses, blood test and scan results, and treatment will be collected and stored in the study database. The referral letter from the GP will include your unique study number so that we can link your primary care and hospital clinical information together in the database.

What will happen to the data after completion of the study?
Your data will be stored and remain codified, but unidentifiable. The data will be maintained for 15 years after the study has been completed, at which point it will be permanently de-identified.

Will I be told of the results of research tests on my samples?
You will be given the results of the routine liver fibrosis tests (Fibroscan or FIB-4 score and ELF test) that are being analysed for this study because these will be used to determine your

risk of having liver fibrosis. You will not receive the results of the experimental biomarker tests because it is not yet known how effective they are. The experimental biomarker tests will not form any part of your medical treatment or record. The overall results of the research project will be presented at scientific meetings and published in the scientific literature. A lay summary of the results will be provided to patient support groups. Your name or any other details that may identify you will not be used in any publications. You have the option to indicate if you would like to receive a brief summary describing the overall results of the SOLID project once it is complete.

What happens if there is a problem?

To ensure participant safety and continual improvements any possible unsatisfactory standards noted during the conduct of the study will be investigated and where required reported to the relevant regulatory authorities.

If you have any concerns or complaints about your participation in the study, you should first talk to your study doctor or a member of the research team, whose contact details are given below.

You can also contact the **Patient Advice Liaison Service (PALS)** on freephone 0800 0320202 or email northoftynepals@nhct.nhs.uk

What if I were harmed during the study?

It is highly unlikely that any harm could come to you in this study. The nurses and doctors involved in the study have all received training and have extensive experience caring for patients with liver disease. If you think you have suffered harm as a result of your participation in the study there are no automatic financial compensation arrangements. However, you may have the right to make a claim for compensation against the Sponsor, Newcastle upon Tyne Hospitals NHS Foundation Trust that is covered by NHS indemnity insurance. If so, you should consider seeking independent legal advice, however, you may have to pay for your legal costs.

Who has reviewed the study?

The London-Chelsea Research Ethics Committee, which has responsibility for reviewing medical research studies, has approved this study.

Who is organising and funding the research?

The study is being sponsored by the NUTH and funded by the Medical Research Council, Clinical Academic Research Partnerships (CARP) funding scheme. Dr Stuart McPherson, consultant Hepatologist at NUTH, is leading the study.

Contact for Further Information

Local Principal Investigator: Dr Mark Dornan
GP

0191 4604239

Other Local Contacts:	Research Nurses: The Newcastle upon Tyne Hospitals NHS Foundation Trust @ nuth.nencnurses@nhs.net
Chief Investigator:	Dr Stuart McPherson The Newcastle upon Tyne Hospitals NHS Foundation Trust Stuart.mcpherson2@nhs.net

For independent information about participating in research studies or to get advice please contact LIVErNORTH (http://www.livernorth.org.uk, Telephone 0191 3702961), the British Liver Trust (http://www.britishlivertrust.org.uk/) or your local Patient Advice and Liaison service.

Thank you very much for taking the time to read and consider your participation in this study.