PARTICIPANT INFORMATION SHEET

Title: **Defining 'normal' liver function tests and FibroScan values in pregnancies with or without liver disease**

Chief Investigator: **Professor Michael Heneghan**

Researchers: **Dr Mussarat Rahim**

Introduction

You are invited to take part in this research study. Before you decide whether you wish to take part, it is important you understand why the research is being done and what it will involve. Please take time to read the following carefully, and if required, discuss it with your friends, family or GP. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

The liver is an important organ that lies in the right-hand side of your abdomen. It is usually protected under the rib cage. It has many important functions, including the production of necessary proteins, the filtering/detoxification of blood and the break-down of important substances which allow your body to function normally. Abnormalities in the liver are therefore important to detect early.

Females that become pregnant can sometimes have underlying liver disease that is unknown to them, and the changes of pregnancy on the body can expose problems within the liver. In addition, pregnant women can develop certain unique liver conditions that are specifically related to pregnancy. Depending on the type or extent of liver disease, there can be effects on the mother, baby and the outcomes of pregnancy. Hence, the early detection of liver disease is crucial in making the right diagnosis and starting any necessary treatments as soon as possible.

Detecting liver disease in pregnant women can be very difficult for several reasons. The blood tests that look at whether your liver is functioning are not routinely performed during pregnancy. They are only done if there is suspicion of liver disease or other conditions. Sometimes liver disease can have no symptoms whatsoever, so it is difficult to say how many pregnant women have or will develop liver disease. In addition, certain tests that look at the liver are not recommended during pregnancy. If possible, a liver biopsy (a technique in which a small sample is taken from the liver) is generally avoided during pregnancy. There need to be better ways to detect liver disease in pregnancy without using tests that pose risk to the mother or the baby.

Transient elastography (FibroScan) is now a well-established test used in the assessment of liver fibrosis (i.e. scarring/stiffness of the liver) in patients with longstanding liver disease, such as hepatitis secondary to viruses. It is a useful way of predicting how much damage there is in the liver, often negating the need for liver biopsy, which has its own complications.

A FibroScan is easily performed at the bedside. It is well-tolerated and takes minutes to perform. It delivers immediate and consistent results, although it does not always get values in all patients.

There is little data on the usefulness of this test in pregnancy. Although it has been available for several years, the use of FibroScan specifically in pregnancy has mainly become popular world-wide over the last two years. However, 'normal' and 'abnormal' values in pregnant patients are based on values in non-pregnant patients. It is important to determine the true normal values specific to pregnancy. Abnormal results may precipitate further investigations during or after pregnancy.

This study will aim to assess the change in liver stiffness measurements during the three trimesters of pregnancy in healthy and more complicated pregnancies. In addition, it will define the normal ranges of liver function tests in blood tests during pregnancy. This data can be compared to normal values in healthy patients who are not pregnant. FibroScan has the potential to detect significant liver disease, even when liver function tests (in blood) are normal. Together, defining normal liver function tests in blood samples and FibroScan values in pregnancy may allow better detection of liver disease in pregnancy and therefore affect the outcome on pregnancy, foetus and mother.

What groups of patients will the study involve?

We are interested in involving any pregnant patient above the age of 16 years, whether they have underlying liver disease or not.

Why have I been invited?

All pregnant patients above the age of 16 years undergoing clinic appointments or routine scans at King's College Hospital NHS Foundation Trust may be eligible to participate in this study. If you have a pacemaker (an electrical device in the heart) we will unfortunately not be able to include you in the study.

Do I have to take part?

No, participation is entirely voluntary. It is up to you whether you wish to take part. If you decide to participate, you will be given this information sheet to keep and asked to sign a consent form. If

you decide to participate, you are still free to withdraw at any point and without giving a reason. This will not affect the medical care that you receive.

Who is organising and funding this study?

The doctor in charge and providing the funding for this study is Professor Michael Heneghan, a specialist in Liver Diseases. It is being sponsored by King's College Hospital NHS Foundation Trust.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee to protect the interests of you as the participant. This study has been reviewed and approved by the North West/Liverpool East Research Ethics Committee. It has also been approved by the Health Research authority. The study has been presented to an Obstetrics 'patient group' called the King's Maternity Voices Partnership, a special group of individuals (including patients) set up to specifically look out for the interests of you as a pregnant individual. All their recommendations were incorporated into the study. The overall feedback from the group was very positive and they appreciate the need for studies like these in pregnancy.

What are the next steps if I take part?

If you decide to take part, you can have the FibroScan straightaway if you want, after your routine appointment or scan. Someone will quickly screen whether you are eligible for the study and they will also go through a consent form with you to sign. This would be a good opportunity to ask any questions that you might have. You will then go through the routine consultation as you normally would with the Obstetrician/midwife. If there are plans for blood tests, we will ask your permission if further liver function tests can be added on to the bloods that you have already had. On your agreement, we may ask for further extra blood tests during later 2 trimesters.

For the FibroScan analysis, we will ask you to lie down on the examination bed and put your right arm behind your head. The examiner will use their fingertips to gently identify a space between your ribs on the right-hand side. When an appropriate place has been found, they will put some gel on the blunt probe (as can be seen in the picture above) of the FibroScan and gently place it on the surface of your skin in between your ribs. Then 10 or more readings will be taken by pressing a button on the FibroScan probe. Each time a reading is taken, you may feel a gentle 'flick' on your skin. This is not painful. The procedure itself should only take a few minutes. We can give you the results straightaway and then you can leave. If there are any abnormal results, we will discuss things with you in more detail before you go.

Ideally, we would like to perform this FibroScan test during each of your three trimesters of pregnancy, along with some blood tests (although this may not be required each time).

Here is a possible schedule of events:

Visit No:	1	2	3 (if necessary)	4 (if necessary)
	During 1st trimester (up to 12 weeks of pregnancy)	During 2nd trimester (12 to 24 weeks of pregnancy)	During 3rd trimester (>24 weeks of pregnancy)	During post-pregnancy phase
Window of flexibility for timing of visits:	Any time during trimester	Any time during trimester	Any time during trimester	In 1st three months of post-partum phase
Eligibility confirmation	✓			
Informed Consent	✓			
Medical History	✓			
Physical Examination	✓			
Adverse Events review	✓	✓	✓	✓
Medication review	✓	✓	✓	✓
FibroScan	✓	✓	If possible	If possible
Blood tests for liver function tests	To be added to routine bloods	To be taken	To be taken if possible	To be taken if possible

What are the side effects and risks of taking part?

There are no significant reported side effects from having a FibroScan. The scientific mechanism behind FibroScan is not thought to have any effect on the baby. In the context of the safety data available to us on FibroScan, there is unlikely to be any risk posed to pregnant participants. There are no medications or radiation involved when having a FibroScan. Although very unlikely,

collecting blood samples from the vein may cause localised pain, bruising, dizziness and very rarely infection at the site of blood test.

What are the possible disadvantages of taking part?

In a proportion of patients, we may be unable to get valid readings due to technical issues. In a very small proportion of patients, we may get false positive or false negative results, which may mean subsequent under or over investigation. We, as doctors, will do our upmost to ensure this does not happen through careful interpretation of the results.

What are the possible benefits of taking part?

This study is being undertaken for educational purposes. You will have the opportunity to contribute to medical research in a clinically important field of Medicine, which may also help others in the future or even yourself in future pregnancies. There is also the potential benefit of identifying serious underlying liver diseases which may require more specialist input during and after your pregnancy. Usually, the earlier you detect these conditions the better the outcome for you and your baby. Identifying long-term liver disease is also important for your lifelong health and may require long term follow up and monitoring, which we can initiate.

What if I lose the ability to provide consent after enrolling to the study?

In the very unlikely event you lose the ability to provide ongoing consent during the study (e.g. due to illness), having been able to provide consent at the start of the study, we will withdraw your participation from the study. Identifiable data collected with consent will be retained and used confidentially in connection with the purposes for which consent was sought at the beginning of the study, or it may potentially be included in further research after the current project has ended. No further data or tissue will be collected, nor any other research procedures carried out on or in relation to the participant.

In the very unlikely event, what if things do not go to plan?

If you have concerns about any aspect of this study, you should speak to a study doctor who will do their best to answer your questions (contact details on last page). If you remain unhappy and wish to escalate things further, you can do so through the NHS Complaints procedure by contacting your local Patient Advice Liaison Service (PALS) office. Details of your local office can be obtained by asking your study doctor, GP or looking on the NHS choices website: http://www.nhs.uk/pages/home.aspx.

Every care will be taken in the course of this study. However, in the unlikely event that you are affected adversely by taking part, compensation may be available.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this.

Will my taking part in this study be kept confidential?

Yes. Once you have consented to take part in the study, the information we collect from the study will remain confidential. Certain information regarding you and your condition will be recorded as part of this study. We will not record any personal identifiable information (name, date of birth or contact details) as part of the research records. All information will be stored anonymously in a password-protected database, or in a file in a secure research office. Only the research team and doctors looking after you will have access to the information.

What will happen to the results of the research study?

When we have results for an adequate number of patients after the study has completed, we plan to publish them in an international journal so that the information can benefit as many people as possible. If you wish, we can provide you with a summary of the results when this is available.

What will happen to any samples that I give?

Every effort will be made to ensure blood samples for the study are taken at the same time as would have occurred normally during your routine clinical care – so that there is as little additional discomfort to you as possible. The amount of blood taken will be less than 5 mls (or < 1 teaspoon). This is a small amount for the body (which contains approximately 5000 mL of blood) and will not adversely affect you. Once the samples have been taken, they will be sent to the Viapath laboratory based at King's College Hospital. The samples will not be sent to any external laboratories and will be disposed of within 72 hours of processing.

Contact details:

Thank you for taking the time to read this information. If there are any other details you would like, please do not hesitate to contact us on the numbers below. If there is no response on these numbers (e.g. out of hours), it is possible to contact the on-call Obstetric or Liver teams – via King's College Hospital Switchboard – who can pass any messages on to the research team involved.

Principle investigator: Dr Mussarat Rahim Tel: 0203299000
Study lead: Professor Michael Heneghan Tel: 0203299000

General Data Protection Regulations

King's College Hospital NHS Trust is the sponsor for this United Kingdom based study. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. King's College Hospital NHS Trust will keep identifiable information about you for 10 years after the study has finished.

As an NHS organisation, we use personally-identifiable information to conduct research to improve health, care and services. As a publicly-funded organisation, we have to ensure that it is in the public interest when we use personally-identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Your rights to access change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information by contacting the study doctors.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). Our Data Protection Officer is Nick Murphy-O'Kane and you can contact them at nick.murphy-okane@nhs.net.

A: Where participants are providing personal data directly i.e. personal data is obtained for the primary purpose of research either verbally or in writing from participants e.g. questionnaires or interviews, or documented by care staff e.g. diagnosis, or obtained from care interventions e.g. laboratory results.

King's College Hospital NHS Trust will collect information from you and your medical records for this research study. King's College Hospital will use your name, NHS number, hospital number, address and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from King's College Hospital NHS Trust and regulatory organisations may look at your medical and research records to check the accuracy of the research study. King's College Hospital will pass these details to King's College Hospital NHS Trust along with the information collected

from you and your medical records. The only people in King's College Hospital NHS Trust who will have access to information that identifies you will be people who need to contact you to discuss the study or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number, hospital number, address or contact details.

King's College Hospital will keep identifiable information about you from this study 10 years after the study has finished.

B. Where data is intended to or likely to be used for future research

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research**.** You may be contacted in the future about other research projects that may interest you.

Your information could be used for research in any aspect of health or care and could be combined with information about you from other sources held by researchers, the NHS or government.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.