Participant Information Sheet

I-TEST: novel biomarkers in pregnancy for early prediction of stillbirth

Longitudinal Cohort

You are invited to take part in a research study. To help you decide whether or not to take part, 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. Talk to others about the study if you wish. Contact us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to take part.

Inclusivity Statement: Our team is committed to making research in pregnancy inclusive. We use terms such as 'woman', 'women', 'maternity', throughout our participant information sheet and study website, publications and social media accounts, to refer to those who are planning to become pregnant, are pregnant, and give birth. We acknowledge that not all people who are pregnant and give birth identify as women. It is important that evidence-based care for maternity, perinatal and postnatal health is inclusive and tailored to an individual's wishes.

What is the purpose of the study?

This study aims to further our understanding of why some babies are stillborn and help us identify new tests that we can offer people in pregnancy to identify babies that might be at risk. Every year, around the world, more than two million babies are stillborn and in many of these cases no clear cause is identified. Our current monitoring looks at pregnant women and babies' health using blood tests, blood pressure and ultrasound scans during pregnancy but we know this does not provide a complete picture.

In pregnancy there are changes in the structure and function of blood vessels throughout the body. These blood vessel changes may lead to complications such as pre-eclampsia, high blood pressure and stillbirth. Looking at what is happening to the blood vessels at the back of the eye can help us know what is happening to blood vessels in the rest of the body. This is a simple, quick and non-invasive test that you may have previously had during a visit to the optician.

The purpose of the study is to find out whether monitoring changes in the eye's blood vessels during pregnancy could be a new way of identifying those at risk of pregnancy complications.

Why have I been invited to take part?

You have been asked to take part as you are currently in early pregnancy (less than 23 weeks). By taking part, you can help us understand how the blood vessels at the back of the eye change during pregnancy and whether this eye test could be used in the future as part of screening for pregnancy complications.

Do I have to take part?

No, it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. Deciding not to take part or withdrawing from the study will not affect the healthcare that you receive, or your legal rights.

What will happen if I take part?

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It is up to you to decide whether or not to take part, but before deciding you might want to discuss this with your family or friends. It's a good idea to think about it for at least 24 hours before deciding to take part. If you would like to take part, a member of the research team will answer any questions that you have about the study, and then ask you to sign a consent form. You can also scan the QR code on the left which will take you to the study website, where you can find further information about the research.

We will ask you to attend 2 study visits at the Royal Infirmary of Edinburgh/Queen's Medical Research Institute (QMRI). The first will be at 12 weeks or 20 weeks (+ / - 3 weeks) of pregnancy, and the second at 36 weeks (+ / - 3 weeks) of pregnancy. We will explain what taking the photos of the back of the eye involves and show you the kind of images we look at. We will ask you some questions about your vision and whether or not you wear glasses and/or contact lenses. The procedure for taking the images is similar to a routine eye test. You will be asked to sit in front of some different devices. You place your chin on the chin rest and look into the device. When in position, pictures of both your eyes will be taken. We might need to use some hydrating eye drops but these are just to hydrate your eyes and they do not dilate your pupils, so you will still be able to drive. We would also ask to measure your eye pressure using a device that has a small, lightweight probe which makes brief, painless contact with the front of your eye. There is **no puff** of air. It takes around 30 minutes to collect all the images and measurements for both your eyes.

We may perform an ultrasound assessment to look at patterns of blood flow in different locations (for example to measure the blood flowing towards your womb and between the placenta and your baby) and to take research images. These are not usually used for clinical care and are part of our research study. In addition, we may invite you to take part in a related research study (the I-TEST-M study) which will allow us to collect some extra measurements to better understand how the cardiovascular system changes in pregnancy.

At the 36-week visit (and at the 12 or 20-week visit if you are also participating in the I-TEST-M research study), we will ask if we can take some blood samples from you for storage and measurement of future new markers of pregnancies at risk of stillbirth. We will need to take about a tablespoon of blood. Whilst we don't yet know what will be measured in the sample, it will only be used in research regarding maternal and baby health. You can still take part in the study if you don't want blood samples taken.

We will collect information about your pregnancy including birth outcomes from your electronic health care records.

After your last study visit you will receive a voucher to thank you for your involvement in our research and as reimbursement for your time. You will receive £20 for the I-TEST study and a further £30 if you also took part in the related I-TEST-M study. If you incur additional travel costs due to attending study visits (including any follow-up visits), please let the research team know and we can reimburse these.

Will there be any follow-up?

We may contact you again to invite you to an additional study visit between 6 and 18 months after the end of your pregnancy. We will also ask permission from you to continue to access your electronic healthcare record to collect information about your health in the future.

The purpose of the collecting this follow-up data is to help us understand how changes to blood vessels that occur during pregnancy are connected to long-term heart and blood vessel health, even after the pregnancy has ended. Your participation in this follow-up is optional – it's up to you whether you want to attend a follow-up visit, and whether you give us permission to collect data about your long-term health.

At the follow-up appointment, we would take a repeat set of images of the backs of your eyes. We would also measure your height, weight, and blood pressure, carry out an ultrasound assessment of your heart, and may measure the "stiffness" of your blood vessels using a small, pen-like device which can detect a pulse at different locations on your body, such as at the neck and groin. We may ask you to unbutton or adjust your shirt, or to slightly lower the waistband or your trousers or skirt, to allow us to take these measurements.

We would ask if we can take further blood samples (about a tablespoon) and collect a urine sample. These are for storage and measurements of markers of blood vessel health. We will ask you if you currently or have previously smoked, and whether you have a family history of heart disease.

We would also ask if you would be happy to wear a simple monitor attached to a blood pressure cuff for a period of 24 hours, whilst going about your normal routine. The monitor is a small box and can either hang on a strap around your neck or be attached to your belt. The cuff automatically inflates every 30 minutes to take a measurement of your blood pressure and blood vessel stiffness. The cuff and monitor are very discreet and can be worn under clothing. You can take the equipment off after 24 hours and return it to us using a prepaid envelope (which we would provide).

You would receive a further £10 voucher as reimbursement for your time and to thank you for attending a follow-up visit.

Is there anything I need to do or avoid?

There are no special precautions that you should take in addition to those you are already taking during pregnancy. Please bring your glasses and/or contact lenses (or spare contact lenses) case to the study visits as well as your most recent prescription from your optician.

What are the possible benefits of taking part?

There are no direct benefits to you taking part in this study, but the results from this study might help to improve the healthcare of patients in the future.

What are the possible disadvantages of taking part?

You will be asked to attend two clinical visits which take time out of your day. The first visit will last about half an hour, and the second visit will last around one hour (to allow for both the eye scan and ultrasound scan of the baby). Travelling to these visits may be uncomfortable, especially in the very late stages of pregnancy. If you also agree to attend a follow-up study visit (between 6 and 18 months after the end of your pregnancy), this appointment will last around one hour.

The measurements we are collecting are mainly non-invasive and so should not cause any discomfort. We will ask to take blood samples from you (at the 36-week visit, at the 12 or 20-week visit if you are participating in the I-TEST-M study, and at the postnatal follow-up visit if you attend this) which can cause bruising.

There is a very small possibility that the pictures of your eyes could reveal an incidental health problem that you or your doctor is unaware of. An appropriately trained member of our research team will examine your eye pictures to look for the presence of any seriously abnormal findings, though occurrences of these are rare. If we were to observe any such findings, we would discuss this with you and inform your GP so that appropriate further tests and treatments could be arranged as necessary. We would also refer you to a specialist eye doctor (ophthalmologist).

If we identify any concerns about your baby or the placenta during the ultrasound scan, they will be explained to you and your clinical team so that you can have any additional treatment or monitoring required. In the unlikely event that we identify any concerning findings from our tests during the follow-up visit, we would inform you and your GP so that appropriate further tests and treatments can be arranged.

What if there are any problems?

In the unlikely event that something goes wrong and you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, please contact:

Patient Advice and Support Service (Part of Citizens Advice Bureaux)
23 Dalmeny Street
Leith
EH6 8PG
0131 510 5510

If you have any complaint about the way that you have been treated you should feel free to discuss this with any member of the research team or with your GP.

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

If you change your mind and don't want to carry on with the study you are free to withdraw at any time. This will not affect your clinical care or your legal rights and you will not have to attend any further research visits. If you do decide to withdraw from the study, we will ask you if we can still use the data and samples that we have collected on you and collect information about your baby's birth and your health from your medical records. You can decide whether or not you are happy with this. You can withdraw by contacting the research team at researchmidwives@nhs.scot, or telephone 0131 242 2480, or via the study website contact us form.

What happens when the study is finished?

The information that we collect for this study will be stored securely for 5 years after the study is finished. Only the researchers involved in this study will see the information and analyse this using computers. The information gathered from this will be made anonymous and shared for research purposes with other medical and scientific researchers, subject to strict laws and University of Edinburgh policies intended to safeguard your privacy. It may be that the findings are considered useful enough to publish in scientific journals or to present at conferences. The blood samples will be destroyed after 10 years.

Will my taking part be kept confidential?

Yes. All the information we collect during the course of the research will be kept strictly confidential and there are strict laws which safeguard your privacy at every stage. Your name and date of birth will be held on secure, password protected devices that have been approved by NHS Lothian IT security and governance, accessible only by the research team.

How will we use information about you?

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

We will collect your Community Health Index (CHI) number. Note that the CHI is a population register, used in Scotland for health care purposes. The CHI number uniquely identifies a person on the index and is personal identifiable information. Your CHI number is being collected to allow us to identify your medical records and ensure that we are collecting data on you and not on another person with the same name and age as you.
Other personal identifiable information collected will include your: initials/ name / date of birth / address / post code/ telephone number / e-mail address. We will also collect information about your baby including the CHI number, date of birth, birthweight and baby sex.

We will store this information, along with your consent form for the study, in a secure study database which has been built using a software called REDCap and which is administered by the University of Edinburgh. 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 assigned instead. We will keep all information

about you safe, secure and anonymised in the Royal Infirmary of Edinburgh and in the secure study database, which only delegated members of the research team can access.

Biological samples will be retained at the end of the study in University ultra-low temperature freezers, and destroyed after ten years. We will retain your name, CHI number, and date of birth on the secure study database with restricted access, to allow us to collect information about your long-term health from your electronic healthcare record. Other digital data will be stored on secure university servers with restricted access for 5 years after the end of the study.

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.

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. You also have the choice whether to let us continue to use the information we have collected from you up to that point.

If you choose to stop taking part in the study, we would like to continue collecting information about your pregnancy and health outcomes from the hospital electronic health record. If you do not want this to happen, please tell us and we will stop.

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

- at 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 researchmidwives@nhs.scot, or
- by contacting a Data Protection Officer.

University of Edinburgh
Data Protection Officer
Governance and Strategic Planning
University of Edinburgh
Old College
Edinburgh EH8 9YL
Tel: 0131 651 4114
dpo@ed.ac.uk

NHS Lothian
Data Protection Officer
NHS Lothian Waverley Gate
2-4 Waterloo Place
Edinburgh EH1 3EG
Tel: 0131 465 5444
Lothian.DPO@nhs.net

What will happen to the results of the study?

The study will be written up as a paper and/or presented at a conference. You will not be identifiable in any published results. A general summary of the study's findings will be available on the study website. If you would like to receive anonymised results at the end of the study, please contact us at researchmidwives@nhs.scot

Who is organising and funding the research?

This study has been organised/ sponsored by the University of Edinburgh and NHS Lothian.

The study is funded by Wellcome Leap. The Wellcome Leap website can be found here.

Who has reviewed the study?

The study proposal has been reviewed by the Wellcome Leap panel. Patients and the public have been involved in reviewing the patient facing material and the consideration of the research questions.

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. A favourable ethical opinion has been obtained from the Brighton and Sussex Research Ethics committee. NHS Management Approval has also been given.

Researcher Contact Details

If you have any further questions about the study, please contact the research team at researchmidwives@nhs.scot or telephone 0131 242 2480.

Independent Contact Details

If you would like to discuss this study with someone independent of the study, please contact Dr Sarah Murray (Clinical Lecturer in Obstetrics) on Sarah.Murray@ed.ac.uk.

Complaints

The NHS Lothian Patient Experience Team is responsible for addressing any compliments, concerns or complaints. If you wish to make a complaint about the study please contact:

Patient Experience Team
2–4 Waterloo Place, Edinburgh, EH1 3EG
feedback@nhslothian.scot.nhs.uk
0131 536 3370

The Patient Advice and Support Service (PASS) is an independent service that provides free advice and support about NHS care. It is a part of the Citizens Advice Bureaux (CAB) service. Further information can be found here. There are several CAB which provide this service across the Lothian area. Please find your local CAB via the website. You will need to enter your postcode to find your local CAB.

Participant ID:

CONSENT FORM

I-TEST: novel biomarkers in pregnancy for early prediction of stillbirth

Please **initial** box

1. I confirm that I have read and understand the information sheet for the above study.

*Date (DD MMM YYYY)	*Version Number

**complete during consent process*

2. I have had the opportunity to consider the information, ask questions and have had these questions answered satisfactorily. ☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason and without my medical care and/or legal rights being affected. ☐
4. I give permission for the research team to access my medical records for the purposes of this research study. ☐
5. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the Sponsor (University of Edinburgh and/or NHS Lothian), from regulatory authorities or from the NHS organisation where it is relevant to my taking part in this research. ☐
6. I give permission for the research team to access my i-test consent form submitted via a secure link from the study REDCap database and administered by the University of Edinburgh. ☐
7. I give permission for my Community Health Index (CHI) number or hospital number to be collected and retained on NHS servers and collected and stored on the REDCap database (via a secure link administered by the University of Edinburgh). ☐
8. I give permission for my personal information (including initials, name, date of birth, address, postcode, telephone number, email address, and consent form) to be retained on NHS servers/ passed to the University of Edinburgh research team for administration of the study. People who do not need to know who you are will not be able to see your name or contact details. I understand my email address may be used for study newsletters and sending me a summary of the research at the end of the study. ☐
9. I agree to my General Practitioner being informed of my participation in the study. ☐
10. I understand that data collected about me during the study may be converted to anonymised data. ☐
11. I agree to give blood samples for storage and future analysis. Yes ☐ No ☐

Participant ID:

Please **initial** box

12. I give permission to the study team to contact me after the end of my pregnancy, for the purpose of arranging a follow-up study visit. Yes ☐ No ☐

13. I agree to give a urine sample for storage and future analysis. Yes ☐ No ☐

14. I give permission for the study team to continue to access my medical records in order to collect data about my long-term cardiovascular health. Yes ☐ No ☐

15. I agree to my anonymised data being used for future ethically approved studies. Yes ☐ No ☐

16. I agree to my anonymised biological samples (blood and/or urine) being used for future ethically approved studies. Yes ☐ No ☐

17. I understand that the data generated and samples collected during this study may be used for future commercial development of products/tests/treatments/biomarkers and I will not benefit financially from this. Yes ☐ No ☐

18. I agree to take part in the above study. ☐

Name of Person Giving Consent	Date	Signature
Name of Person Receiving Consent	Date	Signature

1x original – into Site File; 1x copy – to Participant; 1x copy – into medical record