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Can eye imaging in pregnancy help predict stillbirth?

Submission date 28/09/2025	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 29/09/2025	**Overall study status** Ongoing	
Last Edited 21/04/2026	**Condition category** Pregnancy and Childbirth	

Plain English summary of protocol

Background and study aims
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.

Who can participate?
Pregnant women living in the Lothian area who are aged between 16 and 50 years, and who are pregnant with a single baby, are eligible to take part.

What does the study involve?
Participants will be invited to study visits at one (at around 36 weeks) or two (at around 12 or 20 weeks, and at 36 weeks) timepoints during pregnancy. At these visits, pictures of the backs of each eye will be taken using a specialised camera.
At the 36-week visit, an ultrasound scan will also be carried out to look at the womb, placenta, and baby. A blood test will also be taken at the 36-week visit.
Participants will be invited to one follow-up visit 6-18 months after the birth of their baby. At this visit, further pictures of the backs of the eyes will be taken, as well as non-invasive measurements of the heart and blood vessels, and further samples of blood and urine.

What are the possible benefits and risks of participating?
There will be no direct benefits from taking part in the study, but the results may help to improve the healthcare of pregnant women in the future. None of the measurements taken are

expected to pose any risks to the health of participants or their pregnancies. However, there may be inconvenience associated with having to take time to travel to and attend study visits. The blood tests can sometimes cause minor bruising.
There is a small possibility that the measurements may reveal a health problem that a participant was unaware of. In the unlikely scenario that this does occur, the participant will be referred to receive further medical advice and treatment as appropriate.

Where is the study run from?
The University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
April 2023 to October 2028

Who is funding the study?
1. Wellcome Leap
2. Rosetrees

Who is the main contact?
Prof. Rebecca Reynolds, R.Reynolds@ed.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Rebecca Reynolds

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Additional identifiers

Integrated Research Application System (IRAS)
332944

Central Portfolio Management System (CPMS)
60001

Protocol serial number
AC23144

Study information

Scientific Title
I-TEST: Novel Biomarkers in Pregnancy for Early Prediction of Stillbirth

Acronym
I-TEST

Study objectives
The aim of this study is to assess variability in features of the retinal vasculature during pregnancy between individuals and to describe their longitudinal trajectories over gestation and in the postpartum period.

We aim to assess differences in retinal features and their trajectories between women with healthy pregnancies and those affected by placental dysfunction, in order to identify novel retinal biomarkers for integration into models that are predictive of the risk of stillbirth and future maternal cardiovascular disease.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/11/2023, London - Brighton & Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8140; brightonandsussex.rec@hra.nhs.uk), ref: 23/PR/1187

Study design
Single-centre observational study with two arms

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Stillbirth and pregnancy complications linked to stillbirth risk (pre-eclampsia and fetal growth restriction)

Interventions
This is a single-centre observational study with two parallel cohorts as follows:
1. A longitudinal cohort with serial multimodal retinal imaging at 12 (+/-3) and 36 (+/-3) weeks, or at 20 (+/-3) and 36 (+/-3) weeks, in unselected pregnancies (cohort 1).
2. A cross-sectional cohort with multimodal retinal imaging in late pregnancy obtained at 36 (+/-3) weeks, in a cohort enriched with higher risk pregnancies (cohort 2).

Participants from both cohorts will be invited to a single follow-up visit at 12 (+/-6) months postpartum, for repeat retinal imaging and cardiovascular assessment.

Multimodal retinal imaging will be carried out at each study timepoint for both cohorts, comprising colour fundus photography, scanning laser ophthalmoscopy, optical coherence tomography, and optical coherence tomography angiography.

In addition, at the 36-week study visit for both cohorts, supplementary maternal ultrasound assessments may be carried out including measurements of maternal and fetal Doppler indices and capture of research images of the placenta and fetus. Blood samples will also be collected at this 36-weeks appointment, and stored for future measurement of biomarkers of placental dysfunction, maternal vascular dysfunction, and stillbirth.

Key maternal demographics and maternal and neonatal outcomes for all participants will be collected at birth from the electronic health record.

The 12-month follow up study visit will comprise multimodal retinal imaging as described above, maternal cardiovascular assessment (including verbal report of smoking status and family history of cardiovascular disease, echocardiography, and measurement of height, weight, blood pressure, pulse wave velocity, and 24-hour ambulatory blood pressure and arterial stiffness). We will collect and store postnatal blood samples for measurement of biomarkers of cardiovascular dysfunction and urine samples for analysis of proteinuria (albumin-creatinine ratio) and storage for measurement of other potential biomarkers of cardiovascular dysfunction.

In addition, we will seek consent from participants to collect outcome data on cardiovascular risk factors (including hypertension, diabetes, dyslipidaemia) and future cardiovascular events through lifelong data linkage to GP and hospital records.

Intervention Type
Other

Primary outcome(s)
1. Multimodal retinal imaging (colour fundus photography, scanning laser ophthalmoscopy, optical coherence tomography, and optical coherence tomography angiography) will be carried out at 36 weeks gestation and 12 months postpartum (cohort 1), or at 12 or 20 weeks gestation, 36 weeks gestation, and 12 months postpartum (cohort 2). Automated analysis of retinal images at all timepoints will be carried out to generate retinal vascular metrics including:
1.1. Measures of retinal vessel calibre
1.2. Measures of retinal vessel tortuosity
1.3. Measures of retinal vessel branching complexity
1.4. Measures of choroid thickness and volume
2. Clinical outcome data will be collected postnatally from the medical record for all participants, at least 2 weeks following birth. These will relate to the occurrence of pregnancy complications and birth outcomes, including birthweight, gestation at birth, mode of birth, indication for delivery, neonatal unit admission, respiratory distress, Apgar scores and umbilical cord pH levels. Collection of clinical outcome data will allow us to use the collected retinal imaging-derived measures in predictive outcome modelling for pregnancy complications.

Key secondary outcome(s))
1. Supplementary maternal ultrasound assessment will be carried out at 36 weeks' gestation for participants in both cohorts, and will include measurement of bilateral uterine artery Doppler,

umbilical artery Dopplers, fetal middle cerebral artery Doppler, and capture of B-mode cross-sectional images of the placenta, fetal thorax, and fetal liver.
2. Blood samples will be collected at 36 weeks' gestation for both cohorts, for storage and future measurement of biomarkers of placental dysfunction.
3. At the 12-month postnatal follow up visit, the following supplementary data will be collected in addition to the multimodal retinal imaging previously described:
3.1. Measures of maternal cardiovascular health, including height, weight, blood pressure, pulse wave velocity, and 24 hour ambulatory blood pressure and arterial stiffness
3.2. Self report of smoking status and family history of cardiovascular disease
3.3. Echocardiography, including measurement of cardiac output, left ventricular geometry, and left ventricular systolic and diastolic function
3.4. Blood sample for storage and measurement of markers of cardiovascular dysfunction
3.5. Urine sample for measurement of proteinuria by immunoturbidimetry and storage for future measurement of markers of cardiovascular dysfunction

Completion date
01/10/2028

Eligibility

Key inclusion criteria
1. Age 16-50 years
2. Able to give informed consent
3. Singleton pregnancy
4. 12 (+/- 3) weeks gestation or 20 (+ / - 3) weeks gestation (cohort 1)
5. >23 weeks gestation (cohort 2)
6. Living in Lothian area

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
50 years

Sex
Female

Total final enrolment
0

Key exclusion criteria

1. Women who are not pregnant
2. Women aged under 16 years or over 50 years
3. Women who are classified as Adults with Incapacity (AWI) as determined by midwife, GP or research team
4. Multiple pregnancy

Date of first enrolment
01/12/2023

Date of final enrolment
01/03/2027

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
Scotland
EH16 4SA

Sponsor information

Organisation
Accord (United Kingdom)

ROR
https://ror.org/01x6s1m65

Funder(s)

Funder type
Charity

Funder Name

Wellcome Leap

Alternative Name(s)
Leap, Wellcome Leap Inc, Wellcome Leap, Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United States of America

Funder Name
Rosetrees Trust

Alternative Name(s)
Rosetrees, Teresa Rosenbaum Golden Charitable Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (University of Edinburgh DataStore).

This is a prospective study, and therefore informed participant consent will include provision for data sharing to maximise the value of the dataset for wider research use. The fully anonymised dataset will be available on study close-down with metadata documentation to enable understanding and reuse, upon request from Prof. Rebecca Reynolds (R.Reynolds@ed.ac.uk). All data users will be required to agree to a set of terms for the use of the data, in writing, prior to receipt of the data.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Participant information sheet	version 4.0		29/09/2025	No	Yes
Participant information sheet	version 4.0		29/09/2025	No	Yes
Protocol file	version 4.0	09/12/2024	29/09/2025	No	No
Protocol file	version 5.0	23/02/2026	21/04/2026	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes