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Pregnancy outcome prediction study 2

Submission date 26/09/2019	**Recruitment status** Recruiting
Registration date 07/10/2019	**Overall study status** Ongoing
Last Edited 07/11/2023	**Condition category** Pregnancy and Childbirth

✓ Prospectively registered
? Protocol not yet added
? SAP not yet added
– Results not yet expected
– Raw data not yet expected
✓ Record updated in last year

Plain English Summary
Background and study aims
Screening for pregnancy complications around delivery has not changed very much over the last 30 years. Moreover, we know that the methods currently employed, such as measuring the size of the “bump” with a tape measure, do not perform well

The aims of this trial are:
1. To determine whether a new approach, using ultrasound and blood tests, is effective at picking up high risk pregnancies, and
2. Whether intervening in the pregnancy, based on the result, reduces the risk. Intervention will consist primarily of the offer of earlier delivery by induction of labour

Who can participate?
Women with a singleton pregnancy at the time of their dating ultrasound scan who have not had any previous births

What does the study involve?
We will obtain blood at around 12, 20, 28 and 36 weeks of gestation from the women and blood from the father of the baby (if present and consents) at one of these visits. We will also obtain samples at the time of birth, including placenta, membranes and blood from the umbilical cord. We will collect data from the participants through a questionnaire and by performing ultrasound scans at around 20, 28 and 36 weeks. We will link the research data to the woman's and baby's clinical records. The data and biological samples will provide a resource to develop and validate predictive tests for adverse pregnancy outcome. However, in addition to this, we will also perform a randomised controlled trial. Using data from the Pregnancy Outcome Prediction study, we have developed a test which identifies women at high risk of complications at around eight months of pregnancy (36 weeks). The blood sample, scan information and mother's characteristics will be used to identify women at high risk following the 36 week visit. These women will be randomised to have routine care (meaning that the high risk status will not be revealed) or to have the result revealed with the offer of intervention, principally, early delivery of the baby by induction of labour. The primary outcome of the trial is a composite of either preeclampsia (a pregnancy-specific complication resulting in high blood pressure and other problems) in the mother or growth restriction of the baby

What are the possible benefits and risks of participating?
Participating involves some additional blood tests and these can cause mild discomfort and bruising. One benefit of participating is that we will reveal some scan information when it shows that there is a major problem. For example all women in the study will be told if there baby is in a breech presentation at 36 weeks. This allows time to try and turn the baby or to plan a caesarean delivery. In relation to the women who screen high risk, those who are randomised to having the result revealed and receiving intervention may either experience risks or benefits. We do not know the balance and this is the reason for doing the research. Women who screen high risk where the result is incorrect (i.e. they would have had a normal outcome if left alone) may experience an unnecessary intervention, specifically early induction of labour. However, women who screen high risk where the result is correct may benefit by avoiding complications of pregnancy through earlier delivery, before the complication can happen

Where is the study run from?
The Rosie Hospital, UK

When is the study starting and how long is it expected to run for?
January 2020 to June 2026

Who is funding the study?
Wellcome Trust, UK

Who is the main contact?
Prof. Gordon Smith
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Study website
https://www.obgyn.cam.ac.uk/research/pops-2/pops2/

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
271826

ClinicalTrials.gov number
Nil known

Protocol/serial number
215524/Z/19/Z, IRAS 271826

Study information

Scientific Title
The evaluation and development of novel diagnostic methods to understand and prevent placentally-related complications of human pregnancy

Acronym
POPS2

Study hypothesis
1. Screening nulliparous pregnant women using measurement of sFLT1/PlGF ratio at ~36 weeks of gestational age (wkGA) identifies women at increased risk of placentally-related complications at term
2. Revealing the result of screening using the sFLT1/PlGF ratio at ~36wkGA reduces the risk of maternal and perinatal morbidity and mortality
3. Measurement of other biomarkers in maternal blood may enhance risk prediction of placentally-related complications of pregnancy

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/12/2019, East of England - Essex Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048106; NRESCommittee.EastofEngland-Essex@nhs.net), ref: 19/EE/0331

Study design
Prospective cohort study with nested randomised controlled trial of screening and intervention

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Condition
Pre-eclampsia and fetal growth restriction

Interventions
Women will be recruited at their dating ultrasound scan, typically performed ~12wkGA. Blood will be obtained at this visit, at their anomaly scan (20wkGA), and at two research appointments (28wkGA and 36wkGA) when research ultrasound scans will be performed. At the 36wkGA visit, women will be consented for participation in the RCT element of the study. For those who consent, their risk of term preeclampsia and/or fetal growth restriction will be calculated using a rule derived from the original POP study and based around the sFLT1/PLGF ratio. Women who screen high risk will then be randomly allocated to either having the result revealed or masked. Where the result is masked, there will be no communication of the risk score with the participant and she will continue to receive the standard of care at the Rosie Hospital. Women who screen high risk and are randomised to intervention will be reviewed and their results discussed. They will be offered early delivery, typically induction of labour between 37wkGA and 39wkGA where the clinical management of induction will follow the standard hospital protocols for high risk women.

Both arms will be followed up until the mother is discharged following the hospital admission when she delivered. Randomisation will be with minimisation based on the four elements of the screening assessment.

Randomisation:
The randomisation list will be computer-generated by an independent statistician and provided for incorporation into the study database by the data manager

Intervention Type
Mixed

Primary outcome measure
The primary outcome is a composite, namely, one or more of the following:
1. Diagnosis of preeclampsia (using the ACOG 2013 definition),
2. Perinatal death or perinatal morbidity, or
3. Delivery of an infant with a birth weight <3rd percentile for sex and gestational age

Perinatal death will be defined as stillbirth or neonatal death. Perinatal morbidity is defined as ≥1 of the following: a 5 minute Apgar score <7, delivery with metabolic acidosis (defined as a umbilical cord artery or vein pH <7.1 and a base deficit of >10mmol/L) or admission to the neonatal unit (defined as admission <48 hours after birth and discharge ≥48 hours after admission). We will also study a subgroup of the primary outcome, namely, composite severe adverse outcome. This will be defined as one or more of the following: (i) preeclampsia with severe features (ACOG 2013 definition) (ii) perinatal death or severe perinatal morbidity. Severe

perinatal morbidity will be defined as livebirth associated with hypoxic ischaemic encephalopathy (any grade), use of inotropes, mechanical ventilation, or severe metabolic acidosis (defined as a umbilical cord artery or vein pH <7.0 and a base deficit of >12mmol/L.

Secondary outcome measures
Secondary outcomes will include each of the individual elements of the maternal and perinatal composite described above. The following additional secondary outcomes will be studied:
1. Maternal:
1.1 Maternal death
1.2 Maternal stroke
1.3 Maternal admission to any medical unit (e.g. intensive care unit, stroke unit, coronary care unit, neurosciences critical care unit)
1.4 Placental abruption
1.5 Cord prolapse
1.6 Caesarean section
1.7 Epidural anaesthesia
1.8 Instrumental vaginal delivery
1.9 General anaesthesia
1.10 Post-partum haemorrhage (any >500ml)
1.11 Post-partum haemorrhage requiring blood transfusion
1.12 Infection (pyrexia >38°C and treated with a course of antibiotics)
Maternal death, stroke, admission to a medical unit, hemorrhage and infection will include all episodes occurring prior to discharge home following the delivery.

2. Perinatal:
2.1 Apgar at 1 minute
2.2 Apgar at 5 minutes
2.3 Apgar at 10 minutes
2.4 Umbilical arterial pH and base deficit
2.5 Umbilical vein pH and base deficit
2.6 Any/duration of admission to Special Care
2.7 Any/duration of admission to Neonatal Intensive Care
2.8 Fracture (any)
2.9 Seizures (any)
2.10 Prolonged hypotonia (>2h)
2.11 Abnormal level of consciousness (hyperalert, drowsy, lethargic, stupor, decreased response to pain, coma)
2.12 Tube feeding (any duration)
2.13 Head cooling
2.14 Phototherapy
2.15 Severe hypoglycemia (defined as requiring parenteral treatment or drug therapy)

Overall study start date
10/05/2018

Overall study end date
30/06/2026

Eligibility

Participant inclusion criteria

1. Nulliparous (no previous births >23wkGA)
2. Single viable fetus at the dating ultrasound scan with an ultrasonic estimated gestational age <18wkGA

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
12,150

Participant exclusion criteria
Does not meet inclusion criteria

Recruitment start date
01/01/2020

Recruitment end date
30/06/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Rosie Hospital
Robinson Way
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CB2 0SW

Sponsor information

Organisation

Cambridge University Hospitals NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Website
https://www.cuh.nhs.uk/research-and-development

ROR
https://ror.org/04v54gj93

Organisation
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Sponsor type
University/education

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Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The primary publication arising from the study will report the primary and secondary outcomes of the trial comparing three groups:
1. Women who screened low risk
2. Women who screened high risk but were randomized to routine care, and
3. Women who screened high risk and were randomized to having the result revealed with the offer of intervention
Further publications will arise from the analysis of the study cohort

Intention to publish date
01/09/2026

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No