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Pre-eclampsia prevention by timed birth at term 2 (PREVENT-2): a randomised trial

Submission date
13/10/2025

Recruitment status
Recruiting

Registration date
27/10/2025

Overall study status
Ongoing

Last Edited
13/11/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Preeclampsia (PE) is a medical condition that can develop during pregnancy after 20 weeks of gestation. It is determined by high blood pressure and the presence of protein in the urine or the finding of maternal organ dysfunction. PE is one of the leading causes of maternal and perinatal death and disabilities. There is evidence to suggest some benefits to labour induction at or beyond term in women with PE, including a 67% reduction in perinatal death, an 8% reduction in the rate of caesarean section and a 12% decrease in neonatal intensive care unit admission. However, further evidence is required to establish whether early delivery in women could prevent PE in both the mother and their children. Therefore, the aim of this study is to establish whether screening for PE risk at 35-36 weeks' gestation and planning early-term birth for women at increased risk for PE, can reduce the incidence and severity of the disease as well as adverse pregnancy outcomes.

Who can participate?
Women aged over 16 years with a single pregnancy

What does the study involve?
Participants will be randomly allocated to either the intervention group or the control group. In the intervention group, planned early-term birth will be at 37, 38, 39, 40, or 41 weeks, depending on the women's PE risk, and following induction or by caesarean, as appropriate. Initiation of birth will be by labour induction (by local protocol) or elective caesarean (if indicated or desired by the woman) within the first 2 days of the gestational week, according to local protocol. In the control group birth will await the onset of spontaneous labour or the development of a clinical need for delivery. A subset of participant randomised to each arm will be invited to participate in a sub-study involving postnatal follow-up at six months after birth and all participants will be invited to participate in a qualitative sub-study, consisting of a brief, voluntary online survey and selective individual interviews, before and after birth.

What are the possible benefits and risks of participating?
Participants may benefit from a reduced chance of developing preeclampsia, which could have a

positive impact on the health of both the mothers and the children. There is a risk of pain from the blood collection at two of the clinical visits. There are potential risks from elective caesarean and childbirth.

Where is the study run from?
King's College Hospital, London and Medway Maritime Hosptial (UK)

When is the study starting and how long is expected to run for?
October 2025 to March 2027

Who is funding the study?
The Fetal Medicine Foundation (UK)

Who is the main contact?
Prof. Kypros Nicolaides, Kypros@fetalmedicine.com

Contact information

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Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
357773

Central Portfolio Management System (CPMS)
69853

Study information

Scientific Title
Pre-eclampsia prevention by timed birth at term 2 (PREVENT-2): a randomised trial

Acronym
PREVENT-2

Study objectives
To examine whether screening for pre-eclampsia (PE) risk at 35-36 weeks’ gestation, and offering subsequent risk-stratified care, including timed early term birth for those at higher risk for PE, can reduce the incidence and severity of PE, as well as associated adverse pregnancy outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
submitted 13/10/2025, South East Scotland Research Ethics Service (SESRES) (Waverley Gate, 2 - 4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 131 465 5473; Sandra. Wyllie@nhslothian.scot.nhs.uk), ref: 25/SS/0067

Study design
Open-label multicentre randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Pre-eclampsia

Interventions
Randomisation will be provided by a computer-generated programme hosted by King's Clinical Trials Unit, in random permuted blocks, using a minimisation algorithm to ensure balance in the treatment allocation stratified for participating site.

Intervention group 1: Screening for PE at 35-36 weeks' gestation and risk-stratified care, including timed early term birth.

Screening for PE will be by a combination of maternal factors, MAP, PlGF and sFlt-1. MAP will be measured by validated automated devices and a standardised protocol. Serum sFlt-1 and PlGF concentrations will be measured by an automated device (BRAHMS KRYPTOR compact PLUS, Thermo Fisher Scientific, Hennigsdorf, Germany).

Women with PE risk ≥1 in 100 will have initiation of birth at 39+0-2 by labour induction (by local protocol) or elective caesarean (if indicated or desired by the woman). Those with PE risk <1 in 100 will be offered usual (expectant) care, according to local protocol.

In those at highest risk of developing PE (risk ≥1 in 5), enhanced surveillance will also be undertaken with weekly in-person blood pressure check until delivery in addition to daily home blood pressure monitoring, and a repeat ultrasound scan for fetal growth two weeks after the 35-36 week scan to monitor for any indications to plan delivery prior to intended 39+0-2. At each visit, an additional blood sample will be taken to measure sFlt-1 and PlGF concentrations as part of research. This blood sample will not guide decision for ongoing care including timing of delivery. Blood pressure devices will be provided to those participants for daily blood pressure monitoring. Participants will receive instructions on the use of the device, management according to home blood pressure readings and a diary to record the measurements which will be collected by the study team.

Control group 2: Usual care

No screening for term PE risk will be undertaken at randomisation or prior to birth. Birth will await onset of spontaneous labour or development of a clinical need for birth, as per local policy.

Intervention Type
Procedure/Surgery

Primary outcome(s)

1. Pre-eclampsia at delivery is measured using the 2021 ISSHP definition of pre-eclampsia at the day of delivery
2. Hypertension is measured using systolic and diastolic blood pressure readings taken on at least two occasions four hours apart at the day of delivery
3. Proteinuria is measured using 24-hour urine protein collection, urinary protein-to-creatinine ratio, or dipstick analysis of midstream or catheter urine specimens at the day of delivery
4. Neurological complications are measured using clinical assessment and medical record review at the day of delivery
5. Haematological complications are measured using full blood count and coagulation profile at the day of delivery
6. Pulmonary oedema is measured using clinical examination and chest imaging (e.g. chest X-ray or ultrasound) at the day of delivery
7. Acute kidney injury is measured using serum creatinine levels at the day of delivery
8. Liver involvement is measured using serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels at the day of delivery
9. Uteroplacental dysfunction is measured using estimated fetal weight by ultrasound and Doppler indices (uterine artery PI, umbilical artery PI, middle cerebral artery PI) at the day of delivery

Key secondary outcome(s))

1. Gestational hypertension is measured using blood pressure readings on at least two occasions four hours apart at ≥20 weeks' gestation
2. Components of the 2021 ISSHP definition of pre-eclampsia are measured using clinical and laboratory assessments at the day of delivery
2.1. Pre-eclampsia is measured using the 2019 ACOG definition at the day of delivery
2.2. Gestational hypertension or severe hypertension is measured using blood pressure readings at the day of delivery
2.3. Proteinuria is measured using 24-hour urine collection, protein-to-creatinine ratio, or dipstick analysis at the day of delivery
2.4. In the absence of proteinuria, maternal organ dysfunction is measured using the following:
2.4.1. Pulmonary oedema is measured using clinical examination and imaging at the day of delivery
2.4.2. Platelet count <100 x 10^9/L is measured using full blood count at the day of delivery
2.4.3. Serum creatinine >97 µmol/L or a doubling of baseline is measured using serum biochemistry at the day of delivery
2.4.4. ALT or AST >67 IU/L is measured using liver function tests at the day of delivery
3. Severe features of pre-eclampsia are measured using clinical and laboratory assessments at the day of delivery
3.1. Severe hypertension is measured using blood pressure readings ≥160/110 mm Hg at the day of delivery
3.2. Platelet count <100 x 10^9/L is measured using full blood count at the day of delivery
3.3. ALT or AST >67 IU/L and persistent right upper quadrant or epigastric pain is measured using liver function tests and clinical assessment at the day of delivery
3.4. Serum creatinine >97 µmol/L or doubling of baseline is measured using serum biochemistry at the day of delivery
3.5. Pulmonary oedema is measured using clinical examination and imaging at the day of delivery
3.6. New-onset headache unresponsive to medication is measured using clinical assessment at the day of delivery
3.7. Visual disturbances are measured using clinical assessment at the day of delivery
4. PIERS combined adverse maternal outcome is measured using Delphi consensus criteria and

clinical records at the day of delivery
4.1. Maternal death is measured using hospital records at the day of delivery
4.2. Central nervous system complications are measured using clinical and neurological assessments at the day of delivery
4.2.1. Stroke is measured using neurological assessment and imaging at the day of delivery
4.2.2. Eclampsia is measured using clinical diagnosis of seizures without epilepsy at the day of delivery
4.2.3. Blindness is measured using ophthalmologic assessment at the day of delivery
4.3. Cardiorespiratory complications are measured using clinical and treatment records at the day of delivery
4.3.1. Uncontrolled hypertension is measured using antihypertensive treatment records at the day of delivery
4.3.2. Inotropic support is measured using medication administration records at the day of delivery
4.3.3. Pulmonary oedema is measured using clinical signs, oxygen saturation, diuretic use, or imaging at the day of delivery
4.3.4. Respiratory failure is measured using ventilation and oxygen therapy records at the day of delivery
4.3.5. Myocardial ischemia or infarction is measured using ECG and cardiac biomarkers at the day of delivery
4.3.6. SpO_2 <90% is measured using pulse oximetry at the day of delivery
4.4. Haematological complications are measured using laboratory and transfusion records at the day of delivery
4.4.1. Platelet count <50 x 10^9/L is measured using full blood count at the day of delivery
4.4.2. Blood transfusion is measured using transfusion records at the day of delivery
4.5. Hepatic complications are measured using liver function tests and imaging at the day of delivery
4.5.1. Hepatic dysfunction is measured using INR, bilirubin, and glucose levels at the day of delivery
4.5.2. Hepatic haematoma or rupture is measured using imaging or surgical findings at the day of delivery
4.6. Acute kidney injury is measured using serum creatinine and dialysis records at the day of delivery
4.6.1. Acute serum creatinine >200 µmol/L with pre-existing renal disease is measured using serum biochemistry at the day of delivery
4.6.2. Acute serum creatinine >150 µmol/L with no pre-existing renal disease is measured using serum biochemistry at the day of delivery
4.6.3. Dialysis is measured using renal treatment records at the day of delivery
4.7. Placental abruption is measured using clinical diagnosis or placental examination at the day of delivery
4.8. Other maternal complications are measured using hospital records at the day of delivery
5. Core maternal outcome set for pre-eclampsia is measured using predefined criteria and clinical records at the day of delivery
5.1. Maternal mortality is measured using hospital records at the day of delivery
5.2. Central nervous system complications are measured using clinical and neurological assessments at the day of delivery
5.3. Cardiorespiratory complications are measured using clinical and treatment records at the day of delivery
5.4. Platelet count <100 x 10^9/L is measured using full blood count at the day of delivery
5.5. Hepatic complications are measured using liver function tests and imaging at the day of delivery
5.6. Acute kidney injury is measured using serum creatinine and dialysis records at the day of

delivery
5.7. Placental abruption is measured using clinical diagnosis or placental examination at the day of delivery
5.8. Postpartum haemorrhage ≥1 L is measured using estimated blood loss within 24 hours after birth
5.9. Maternal admission to intensive care or high dependency unit is measured using hospital admission records at the day of delivery
6. Severe hypertension is measured using blood pressure readings ≥160/110 mm Hg at the day of delivery
7. Caesarean section (any) is measured using clinical records at the day of delivery
8. Labour onset is measured using clinical records and classified as spontaneous, induced, or no labour at the day of delivery
9. Maternal admission to intensive care or high dependency unit is measured using hospital admission records at the day of delivery
10. Total number of nights in hospital is measured using hospital admission and discharge records at discharge
11. Gestational age at delivery is measured using ultrasound dating and delivery records at the day of delivery
12. Stillbirth is measured using delivery records at the day of delivery
13. Birthweight <3rd, <5th, and <10th percentile is measured using birthweight and Fetal Medicine Foundation charts at the day of delivery
14. Neonatal death is measured using neonatal records up to 28 days of life
15. Admission to neonatal care unit (any duration) is measured using neonatal admission records at discharge or 28 days of life
16. Neonatal morbidity is measured using clinical and diagnostic records up to 28 days of life
16.1. Intraventricular haemorrhage grade II or above is measured using cranial ultrasound or MRI up to 28 days of life
16.2. Neonatal sepsis is measured using positive blood cultures up to 28 days of life
16.3. Neonatal encephalopathy is measured using clinical grading and head cooling records up to 28 days of life
16.4. Neonatal seizures are measured using clinical observation and EEG up to 28 days of life
16.5. Neonatal anaemia requiring transfusion is measured using haemoglobin/haematocrit and transfusion records up to 28 days of life
16.6. Respiratory distress syndrome is measured using clinical diagnosis and ventilation records up to 28 days of life
16.7. Necrotising enterocolitis requiring surgery is measured using surgical records up to 28 days of life
16.8. Composite neonatal morbidity is measured using presence of any listed neonatal complications up to 28 days of life
17. Neonatal therapy is measured using clinical and treatment records up to 28 days of life
17.1. Neonatal intensive care unit admission is measured using neonatal admission records up to 28 days of life
17.2. Neonatal ventilation is measured using respiratory support records up to 28 days of life
17.3. Composite neonatal therapy is measured using presence of any listed neonatal interventions up to 28 days of life

Completion date
01/10/2027

Eligibility

Key inclusion criteria
1. Singleton pregnancy
2. Live fetus at 35+0-36+6 weeks' gestation
3. Able to provide informed and documented consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
60 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Age <16 years
2. Women with established PE
3. Known major fetal abnormality
4. Participating in another intervention study that influences outcomes of this study

Date of first enrolment
01/11/2025

Date of final enrolment
01/03/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College Hospital
Harris Birthright Centre
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Study participating centre
Medway NHS Foundation Trust
Medway Maritime Hospital
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Sponsor information

Organisation
King's College Hospital NHS Foundation Trust

ROR
https://ror.org/01n0k5m85

Funder(s)

Funder type
Charity

Funder Name
Fetal Medicine Foundation

Alternative Name(s)
FMF

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

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes