ISRCTN41632964 https://doi.org/10.1186/ISRCTN41632964

Preeclampsia prevention by timed birth at term

Submission date
01/11/2022

Recruitment status
No longer recruiting

Registration date
02/11/2022

Overall study status
Completed

Last Edited
27/02/2026

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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 usual antenatal care. The intervention involves screening for pre-eclampsia (PE) at 35-36 weeks of gestation by the competing risk model (combination of maternal characteristics, mean arterial pressure, maternal serum PlGF and sLFT-1) and planned early-term birth at 37, 38, 39, 40, or 41 weeks, depending on the women's PE risk.

What are the possible benefits and risks of participating?
We don't anticipate any benefit or risk for the participants in the expectant group. However, we hope that the intervention will result in a reduction in the incidence of preeclampsia and its associated morbidity. A subgroup of women in the intervention group will have earlier delivery at term. This can be either by cesarean section or induction of labour. There is evidence now to suggest that such induction of labour is not associated with an increased risk of emergency cesarean section, but rather a decrease. A potential risk from earlier delivery might be an increase in the incidence of neonatal unit admission, but we do not anticipate an increase in the rate of neonatal morbidity.

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

When is the study starting and how long is expected to run for?
May 2023 to May 2025

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

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

Contact information

Type(s)
Scientific

Contact name
Miss Angel Leung

Contact details
Harris Birthright Research Centre for Fetal Medicine
King's College Hosptial
London
United Kingdom
SE5 8BB
+44 (0)7857306268
angel.leung2@nhs.net

Type(s)
Scientific

Contact name
Prof Kypros Nicolaides

Contact details
Harris Birthright Research Centre for Fetal Medicine
King’s College Hospital
London
United Kingdom
SE5 8BB
+44 (0)2032998256
Kypros@fetalmedicine.com

Type(s)
Scientific

Contact name
Dr Argyro Syngelaki

Contact details

Harris Birthright Research Centre for Fetal Medicine
King’s College Hospital
London
United Kingdom
SE5 8BB
+44 (0)2032997164
argyro.syngelaki@nhs.net

Type(s)
Scientific

Contact name
Dr James Goadsby

Contact details
Harris Birthright Research Centre for Fetal Medicine
King’s College Hospital
London
United Kingdom
SE5 8BB
+44 (0)2032998256
james.goadsby@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
315444

ClinicalTrials.gov (NCT)
Nil known

Central Portfolio Management System (CPMS)
54393

Study information

Scientific Title
Preeclampsia prevention by timed birth at term: a randomised trial

Study objectives
To determine the effect of screening and timing of delivery on the incidence of delivery with preeclampsia (PE).

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 05/04/2023 , London-Surrey Borders Research Ethics Committee (The Old Chapel, Royal Standard Place, NG1 6FS, UK; +44 (0)207 1048 088; surrey.rec@hra.nhs.uk), ref: 22/LO /0794

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

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

Interventions
Current interventions as of 27/02/2026:
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 sites. Intervention group: Screening for PE at 35-36 weeks' gestation (by a combination of maternal factors, MAP, PlGF and sFlt-1) and planned early-term delivery if the risk for PE is increased, at a risk of at least 1 in 50. Screening for PE will be undertaken by the 'competing-risks model' FMF algorithm that combines maternal demographics and medical history, MAP and maternal serum sFlt-1 and PlGF to provide a personalised risk of PE. 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 will have a planned initiation of early-term delivery, according to their risk of PE, as follows:

Intervention group:
PE risk ≥1 in 2 will have planned delivery at 37+0 - 37+2 weeks
PE risk 1 in 3 to 1 in 5 will have planned delivery at 38+0 - 38+2 weeks
PE risk 1 in 6 to 1 in 20 will have planned delivery at 39+0 – 39+2 weeks
PE risk 1 in 21 to 1 in 50 will have planned delivery at 40+0 – 40+2 weeks
PE risk <1 in 50 will have planned delivery at 41+ weeks (per local policy)

Control group: Usual care
Birth will await the onset of spontaneous labour or development of a clinical need for delivery, as per relevant NICE or RCOG clinical guidance on the timing of birth in general (ng207) or specific to maternal or fetal conditions (e.g., NG133 for pregnancy hypertension)

Previous 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 (by a combination of maternal factors, MAP, PlGF and sFlt-1) and planned early-term delivery if the risk for PE is increased, at a risk of at least 1 in 50.

Screening for PE will be undertaken by the 'competing-risks model' FMF algorithm that combines maternal demographics and medical history, MAP and maternal serum sFlt-1 and PlGF, to provide a personalised risk of PE. 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 will have a planned initiation of early-term delivery, according to their risk of PE, as follows:

In the intervention arm, 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.

Control group 2: Usual care
Birth will await the onset of spontaneous labour or development of a clinical need for delivery, as per relevant NICE or RCOG clinical guidance on the timing of birth in general (ng207) or specific to maternal or fetal conditions (e.g., NG133 for pregnancy hypertension)

Trial timeline:
11-13 weeks – normal routine care and study information provided
20-22 weeks – normal routine care and study information provided
35-36+6 weeks – normal routine care and study information provided (randomisation if participants are eligible and consented to participant)

Intervention Type
Other

Primary outcome(s)
Delivery with PE as defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP) 2021.14. The definition of PE is chronic hypertension or new onset hypertension (systolic blood pressure (BP) should be ≥140 mm Hg and/or diastolic ≥90 mm Hg, on at least two occasions four hours apart BP >140/90 mm Hg) ≥ 20 weeks of gestation together with any of the following:
1. Proteinuria, defined as ≥300 mg in 24 hours or urinary creatinine ratio ≥30 mg/mmol (0.3 mg /mg) or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimens if no 24-hour collection is available; or
2. Maternal organ dysfunction, defined as any one of the following:
2.1. Acute kidney injury with creatinine >90 µmol/l or
2.2. Liver involvement with elevated transaminases (alanine or aspartate aminotransferase [ALT or AST] >40 IU/L or twice the normal concentration) or
2.3. Haematological complications (thrombocytopaenia with platelet count <150 x 109/L), disseminated intravascular coagulation or haemolysis, or
2.4. Neurological complications, such as eclampsia, altered mental status, blindness, stroke, clonus, severe headaches, or persistent visual scotomata, or
3. Uteroplacental dysfunction, defined as estimated fetal weight (EFW) <3rd percentile or EFW at the 3rd to 10th percentile in the presence of either of the following: uterine artery pulsatility index (UtA-PI) >95th percentile, umbilical artery PI (UA-PI) >95th percentile, or middle cerebral artery PI (MCA PI) <5th percentile

All outcome measures will be recorded during the routine care appointment and during childbirth. When the participants do not gIve birth at the chosen hospital, then the outcome is taken from their medical record.

Key secondary outcome(s))

All outcome measures will be recorded during the routine care appointment and during childbirth. When the participants do not gIve birth at the chosen hospital, then the outcome is taken from their medical record.

1. Emergency caesarean section, defined as any caesarean section after spontaneous onset or induction of labour. A caesarean section without prior labour will be considered as elective
2. Neonatal care unit stay for ≥48 consecutive hours up to primary hospital discharge home or 28 days of life, whichever is earlier

Other secondary outcomes:
1. GH, defined as systolic BP ≥140 mm Hg and/or diastolic ≥90 mm Hg, on at least two occasions 4 hours apart, and developing at ≥20 weeks' gestation in previously normotensive women (i.e., BP <140/90 mm Hg)
2. Components of the 2021 ISSHP definition of PE (as above)
2.1. PE as defined by ACOG 201915:
2.2. GH (as above) or severe hypertension (as below), and either
2.3. Proteinuria (as above) or
2.4. In absence of proteinuria, one/more of:
2.4.1. Pulmonary edema
2.4.2. Platelet count <100 x 10e9/litre)
2.4.3. Serum creatinine >97 µmol/L or a doubling in its value
2.4.4. Abnormal liver enzymes (ALT or AST >67 IU/litre)
3. 'Severe features' of PE (one or more), and its components, according to ACOG 201915 and without alternative diagnoses:
3.1. Severe hypertension (as defined below)
3.2. Platelet count <100 x 10e9/L
3.3. ALT or AST raised to twice normal (>67 IU/L) and persistent severe right upper quadrant abdominal or epigastric pain unresponsive to medication and not otherwise accounted for by alternative diagnoses
3.4. Serum creatinine >97 µmol/L or a doubling of value in the absence of other renal disease
3.5. Pulmonary edema
3.6. New-onset headache unresponsive to medication
3.7. Visual disturbances
4. Preeclampsia Integrated Estimate of Risk Score (PIERS) combined adverse maternal outcome, and its components, derived from Delphi consensus (with the exception of the Glasgow coma score <13):
4.1. Maternal death
4.2. Central nervous system complications (one or more of):
4.2.1. Stroke (acute neurological event with deficits lasting > 24 hr, not due to a post-ictal state)
4.2.2. Eclampsia (generalized convulsion in the absence of a history of epilepsy)
4.2.3. Blindness (either retinal or cortical, defined as loss of visual acuity in the presence of intact pupillary response to light)
4.3. Cardiorespiratory complications (one or more of):
4.3.1. Uncontrolled hypertension (requiring administration of 3 or more different parenteral [intravenous or intramuscular] antihypertensive agents within a 12-hour period)
4.3.2. Inotropic support (use of vasopressors to keep systolic BP >90 mmHg or a MAP >70 mmHg)

4.3.3. Pulmonary oedema (diagnosed clinically with one/more of oxygen saturation < 95%, diuretic treatment or x-ray confirmation)
4.3.4. Respiratory failure (intubation, ventilation by endotracheal tube or non-invasively, or need for > 50% oxygen for > 1 hr which is not due to caesarean delivery)
4.3.5. Myocardial ischemia or myocardial infarction (by characteristic ECG changes and markers of myocardial necrosis)
4.3.6. SpO_2 <90%
4.4. Haematological complications (one or more of):
4.4.1. Platelet count <50 x 10e9/L
4.4.2. Transfusion (of any blood product)
4.5. Hepatic complications (one or more of):
4.5.1. Dysfunction (INR>1.2 in the absence of DIC or treatment with warfarin, OR, in the presence of DIC or treatment with warfarin: either mixed hyperbilirubinemia >17 μM or hypoglycemia <2.5 mM) in the absence of insulin)
4.5.2. Hepatic haematoma or rupture (presence of a blood collection under the hepatic capsule as confirmed by imaging or at laparotomy)
4.6. Acute kidney injury:
4.6.1. Acute serum creatinine >200 μM with pre-existing renal disease
4.6.2. Acute serum creatinine >150uM with no pre-existing renal disease
4.6.3. Dialysis
4.7. Placental abruption (clinically or on placental examination)
4.8. Other (as detailed, with appropriate information from hospital records)
5. Core maternal outcome set for PE17 (one or more of) and its components:
5.1. Maternal mortality
5.2. Central nervous system complications: eclampsia, stroke, blindness that is retinal or cortical (as defined for PIERS)
5.3. Cardiorespiratory complications: pulmonary edema, respiratory failure (as defined for PIERS)
5.4. Platelet count <100 x 10e9/L
5.5. Hepatic complications: AST or ALT raised to twice normal, or haematoma (as for PIERS)
5.6. Acute kidney injury (as for PIERS)
5.7. Placental abruption
5.8. Postpartum haemorrhage (defined as blood loss ≥1 L within the first 24 hours after birth)
5.9. Maternal admission to intensive care or high dependency unit
6. Severe hypertension (defined as systolic BP ≥160 mm Hg and/or diastolic BP ≥110 mm Hg, on at least one occasion)
7. Caesarean section (any)
8. Labour onset, classified as spontaneous, induced, or no labour. (Spontaneous rupture of membranes without labour will be considered as spontaneous labour onset)
9. Maternal admission to intensive care or high dependency unit
10. Total number of nights in hospital
11. Gestational age at delivery
12. Stillbirth
13. Birthweight <3rd, <5th and <10th percentile for gestational age, calculated using the Fetal Medicine Foundation birthweight chart
14. Neonatal death (after birth or within the first 28 days of life)
15. Admission to neonatal care unit (for any duration)
16. Neonatal morbidity:
16.1. Intraventricular haemorrhage grade II or above, defined as bleeding into the ventricles
16.2. Neonatal sepsis (defined as confirmed bacteraemia in cultures)
16.3. Encephalopathy grade (mild, moderate, severe) requiring head cooling
16.4. Neonatal seizures
16.5. Anaemia defined as low haemoglobin and/or haematocrit requiring blood transfusion

16.6. Respiratory distress syndrome, defined as the need for ventilation with or without surfactant
16.7. Necrotising enterocolitis requiring surgical intervention
16.8. Composite of any of the above
17. Neonatal therapy:
17.1. Neonatal intensive care unit admission
17.2. Ventilation, defined as the need for positive pressure (continuous positive airway pressure) or nasal continuous positive airway pressure (NCPAP) or intubation
17.3. Composite of any of the above

Completion date
10/05/2025

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
55 years

Sex
Female

Total final enrolment
8000

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 the outcomes of this study

Date of first enrolment
09/05/2023

Date of final enrolment
21/11/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
King's College Hospital
16-20 Windsor WalK
London
England
SE5 8BB

Study participating centre
Medway Maritime Hospital Laboratory
Medway Maritime Hospital
Windmill Road
Gillingham
England
ME7 5NY

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?
Results article		04/12/2025	18/12/2025	Yes	No
Protocol article		10/04/2025	14/04/2025	Yes	No