ISRCTN77258279 https://doi.org/10.1186/ISRCTN77258279

When to induce labour to limit risk in pregnancy hypertension

Submission date	Recruitment status	[X] Prospectively registered
01/11/2018	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/12/2018	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/06/2025	Pregnancy and Childbirth	

Plain English summary of protocol

Background and study aims

This study is looking to enrol pregnant women who have high blood pressure (hypertension) during their pregnancy. High blood pressure increases the risk of harm to the mother and to her baby, and the study is being conducted to see when it is best to deliver the baby in order to minimise this risk as much as possible. In the UK, up to 55,000 pregnant women each year have high blood pressure during their pregnancies. It is not known whether delivery should be started before the onset of spontaneous labour that usually occurs at term, defined as 37-42 weeks (within which is the 'due date' of 40 weeks of pregnancy). Early planned delivery at term (at 37-38 weeks) may reduce stillbirth and complications for the mother, such as separation of the placenta from the wall of the womb, or development of pre-eclampsia, a more concerning form of high blood pressure that is associated with protein in the urine or other problems for mothers and babies and possibly Caesarean delivery. However, early planned delivery at term may also cause harm, including newborn health problems such as breathing or other difficulties that may require the baby to need care in a newborn unit. This study is looking at the experiences of 1,080 pregnant women with hypertension who have been pregnant for at least 36 to 37 weeks to see if delivering their baby between 38 weeks plus zero days to 38 weeks plus 3 days gives a better outcome for the mother and her baby than does waiting for at least 40 weeks for the women to deliver. At the moment there is no conclusive evidence to say which delivery time is best. Different doctors do different things and this is why this study is needed.

Who can participate?

Women aged 16 years and over who are 36 to 37 weeks pregnant and have hypertension

What does the study involve?

Participants are randomly allocated to planned birth at 38 weeks, or planned observation of pregnancy until at least 40 weeks (unless an indication for birth develops). The research midwife contacts participants weekly until the birth. Before leaving hospital after birth, participants are asked to complete a two-page questionnaire about their experience of childbirth. At 6 weeks after birth, they are sent a very brief online questionnaire via a text message, to find out about any serious problems that the mothers or babies may have experienced since leaving hospital after birth. There is support throughout from dedicated research midwives.

What are the possible benefits and risks of participating?
Mothers and babies are closely monitored. The knowledge gained from this research might in the future benefit many, many women with high blood pressure in pregnancy. The study involves no new interventions and has no added risks to the mother or baby; instead, the study measures risk.

Where is the study run from?
1. Guy's and St Thomas' NHS Foundation Trust (UK)
2. Leeds Teaching Hospitals NHS Trust (UK)
3. Liverpool Women's Hospital (UK)
4. Birmingham Women's Hospital (UK)
5. West Middlesex Hospital (UK)
6. Croydon University Hospital (UK)
7. Leicester Royal Infirmary (UK)
8. Nottingham City Hospital (UK)
9. Queen's Medical Centre (UK)
10. Princess Anne Hospital (UK)
11. St Mary's Hospital (UK)
12. Poole Hospital (UK)
13. Norfolk & Norwich University Hospital NHS Foundation Trust (UK)
14. York Hospital (UK)
15. Singleton Hospital (UK)
16. North West Anglia NHS Foundation Trust (UK)
17. Royal United Hospital, Bath (UK)
18. South Tees Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2018 to January 2024

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
Katie Kirkham
will@trials.bham.ac.uk

Study website
https://www.birmingham.ac.uk/research/bctu/trials/womens/will/will

Contact information

Type(s)
Scientific

Contact name
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will@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
252294; HTA 16/167/123

Study information

Scientific Title
When to Induce Labour to Limit risk in pregnancy hypertension - a multi-centre, randomised controlled trial in women with chronic or gestational hypertension

Acronym
WILL

Study objectives
Earlier delivery at term may be beneficial to women with chronic or gestational hypertension, without increasing risk to babies or caesarean delivery.

The trial will investigate the clinical effectiveness and cost-consequences of planned early term delivery at 38+0 to 38+3 weeks gestation, compared with expectant care at term until at least 40+0 weeks gestation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/01/2019, London - Fulham Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, Tel: +44 (0)207 104 8021; Email: nrescommittee.london-fulham@nhs.net), REC ref: 18/LO/2033, Protocol number: 252294, IRAS project ID: 252294

Study design
Open-label interventional multicentre non-blinded study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
https://www.birmingham.ac.uk/research/bctu/trials/womens/will/investigators/documentation

Health condition(s) or problem(s) studied
Chronic or gestational hypertension that develops by 37+6 weeks gestation

Interventions
Current interventions as of 07/07/2023:
Randomisation will be provided through a bespoke database provided by BCTU.
1. Planned early-term delivery at 38+0 to 38+3 weeks by labour induction (local protocol) or elective Caesarean (if previously indicated)
2. Usual care at term until, with maternal and fetal monitoring (local protocol), awaiting spontaneous labour or delivery indicated by clinical need (e.g., refractory severe hypertension or pre-eclampsia)

Follow-up: 31/11/2018 to 31/01/2023.

Previous interventions:
Randomisation will be provided through a bespoke database provided by BCTU.

1. Planned early-term delivery at 38+0 to 38+3 weeks by labour induction (local protocol) or elective Caesarean (if previously indicated)
2. Expectant care at term until at least 40+0 weeks, with maternal and fetal monitoring (local protocol), awaiting spontaneous labour or delivery indicated by clinical need (e.g., refractory severe hypertension or pre-eclampsia)

Follow-up: 31/11/2018 to 20/04/2022.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Maternal co-primary outcome: Composite of poor maternal outcome until primary hospital discharge home or 28 days after delivery birth (whichever is earlier), defined as:
1.1. Severe hypertension (i.e., systolic BP (sBP) ≥160 or diastolic BP ≥110mmHg); or
1.2. Maternal death; or
1.3. Maternal morbidity defined as any of the following: GCS<13; stroke; TIA; eclampsia; blindness; uncontrolled hypertension; inotropic support; pulmonary oedema; respiratory failure; SpO2 <90%; myocardial ischaemia or infarction; hepatic dysfunction, hepatic haematoma or rupture; acute kidney injury or dialysis; platelet count <50x109/L; transfusion; or placental abruption. These were adapted from a Delphi consensus in hypertensive pregnancy.
Measured by review of maternity notes/electronic records until primary hospital discharge home

or 28 days after birth (whichever is earlier)
2. Neonatal co-primary outcome: Neonatal care unit admission for ≥ 4 hours, measured by review of maternity or neonatal notes/electronic records until primary hospital discharge home or 28 days after delivery birth (whichever is earlier)

Secondary outcome measures

Maternal:
1. Caesarean delivery, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
2. Instrumental vaginal delivery or Caesarean delivery (vs. spontaneous vaginal delivery), measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
3. Individual components of maternal co-primary outcome, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
4. Elevated liver enzymes, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
5. Platelet count <100x109/L, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
6. Pre-eclampsia, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
7. Sepsis, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
8. Postpartum haemorrhage (PPH), measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
9. Intensive care unit (ITU) admission, measured by review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)

Potential co-interventions (only among women randomised):
1. Antihypertensive therapy taken, measured using review of maternity notes/electronic records ntil uprimary hospital discharge home or 28 days after birth (whichever is earlier)
2. Magnesium sulphate, measured using review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
3. Bedrest at home, measured using review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
4. Use of home BP monitoring, measured using review of maternity notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
5. Maternal blood/urine testing at lab before delivery admission, measured using review of maternity notes/electronic records after randomisation before birth
6. Office/clinic visits, measured using review of maternity notes/electronic records after randomisation before birth
7. Obstetrical day unit visits, measured using review of maternity notes/electronic records after randomisation before birth
8. Acute care visits, measured using review of maternity notes/electronic records after randomisation before birth
9. Antenatal admissions, measured using review of maternity notes/electronic records after randomisation before birth
10. Fetal cardiotocography, measured using review of maternity notes/electronic records after randomisation before birth
11. Fetal ultrasound, measured using review of maternity notes/electronic records after randomisation before birth

1. Clinical indications for delivery in the expectant care arm, measured using review of maternity notes/electronic records after randomisation before birth
2. Maternal satisfaction, measured using Childbirth Experience Questionnaire 2.0 until primary hospital discharge home or 28 days after birth (whichever is earlier)
3. 'Poor maternal outcome'‡, measured using review of maternity notes/electronic records and postpartum questionnaire at 6 weeks after birth
4. Infection of the Caesarean wound, episiotomy or vaginal tear, as applicable‡, measured using postpartum questionnaire at 6 weeks after birth

Neonatal:
1. Neonatal care unit admission, measured using review of maternity or neonatal notes /electronic records and 6 week postpartum questionnaire until 28 days after birth
2. Indication for neonatal care unit admission ≥ 4 hours, measured using review of neonatal notes /electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
3. Respiratory morbidity, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
4. Hypoxic-ischaemic encephalopathy (HIE), measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
5. Sepsis, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
6. Major operation, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
7. Intra-uterine fetal death, assessed by ultrasound doppler antepartum and lack of vital signs at birth
8. Neonatal death, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
9. Breastfeeding established, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)
10. Exclusive breastfeeding, measured using review of neonatal notes/electronic records until primary hospital discharge home or 28 days after birth (whichever is earlier)

Health Economics
Cost-consequence analysis from NHS perspective, measured using review of neonatal notes /electronic records for individual-level data until primary hospital discharge home or 28 days after birth (whichever is earlier)

‡ Only among women randomised

Overall study start date
01/06/2018

Completion date
31/01/2024

Eligibility

Key inclusion criteria
1. Maternal age ≥16 years
2. Diagnosis of chronic or gestational hypertension
3. Singleton pregnancy

4. Live fetus
5. Gestational age of 36+0 to 37+6 weeks
6. Able to give written informed consent to participate

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
1080

Total final enrolment
403

Key exclusion criteria
1. Contraindication to either one of the trial arms (e.g., evidence of pre-eclampsia)
2. Severe hypertension [i.e., blood pressure (BP) ≥160mmHg systolic or ≥110mmHg diastolic] until BP falls below this level (i.e. it is 'controlled')
3. Major fetal anomaly anticipated to require neonatal unit admission
4. Participation in another timing of delivery trial
NOTE: Women with co-morbidities (e.g., diabetes) and fetal size will not be exclusion criteria

Date of first enrolment
03/06/2019

Date of final enrolment
30/04/2022

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre

Guy's and St Thomas' NHS Foundation Trust
R&D Department 16th Floor, Tower Wing
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Leeds Teaching Hospitals NHS Trust
Leeds
United Kingdom
LS9 7TF

Study participating centre
Liverpool Women's Hospital
Crown St
Liverpool
United Kingdom
L8 7SS

Study participating centre
Birmingham Women's Hospital
Mindlesohn Way
Birmingham
United Kingdom
B15 2TG

Study participating centre
West Middlesex Hospital
Twickenham Rd
Isleworth
United Kingdom
TW7 6AF

Study participating centre
Croydon University Hospital
530 London Road
Croydon
United Kingdom
CR7 7YE

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Nottingham City Hospital
Hucknall Rd
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Queen’s Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Princess Anne Hospital
Coxford Rd
Southampton
United Kingdom
SO16 5YA

Study participating centre
St Mary's Hospital
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Poole Hospital
St Mary's Rd
Poole

United Kingdom
BH15 2BH

Study participating centre
Norfolk & Norwich University Hospital NHS Foundation Trust
Colney Ln
Norwich
United Kingdom
NR4 7UY

Study participating centre
York Hospital
Wigginton Rd
York
United Kingdom
YO31 8HE

Study participating centre
Singleton Hospital
Sketty Ln
Sketty
Swansea
United Kingdom
SA2 8QA

Study participating centre
North West Anglia NHS Foundation Trust
Parkway Hinchingbrooke
Huntingdon
United Kingdom
PE29 6NT

Study participating centre
North West Anglia NHS Foundation Trust
Edith Cavell Campus
Bretton Gate
Peterborough
United Kingdom
PE3 9GZ

Study participating centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook Hospital
Marton Rd
Middlesbrough
United Kingdom
TS4 3BW

Sponsor information

Organisation
King's College London

Sponsor details
Room 5.31, James Clerk Maxwell Building
57 Waterloo Road
London
England
United Kingdom
SE1 8WA

Sponsor type
University/education

Website
http://www.kcl.ac.uk/index.aspx

ROR
https://ror.org/0220mzb33

Organisation
Guy's and St Thomas' NHS Foundation Trust

Sponsor details
R&D Department
16th Floor, Tower Wing

Great Maze Pond
London
England
United Kingdom
SE1 9RT
+44 (0)20 7188 7188; Int: 54462
R&D@gstt.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.guysandstthomas.nhs.uk/Home.aspx

ROR
https://ror.org/00j161312

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Results of this trial will be submitted for publication in peer-reviewed journals. The manuscript will be prepared by the TMG; all contributors to the trial will be listed, with their contribution identified and specifically, all collaborating site teams will be listed in an Appendix as the 'WILL Study Group'. Abstracts will be submitted to international medical congresses. Trial participants will be able to access the final results of the trial via the trial website. All publications

/presentations that use data from this trial to undertake original analyses will be submitted to the Funders for review before release; these must be submitted in a timely fashion and in advance of being submitted for publication, to allow time for review and resolution of any outstanding issues.
On all publications, the authors must acknowledge that the trial was: (i) performed with the support of The UofB BCTU, King's College London, and Guy's and St. Thomas' Foundation NHS Trust; and (ii) funded by the NIHR. To safeguard the scientific integrity of the trial, data from this trial will not be presented in public

Intention to publish date
31/01/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Laura Magee (laura.a.magee@kcl.ac.uk), anonymised data will be shared at the end of the trial.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Adaptations to trial during COVID pandemic	21/10/2022	24/10/2022	Yes	No
HRA research summary			28/06/2023	No	No
Protocol article		03/04/2023	30/05/2024	Yes	No
Results article		26/11/2024	28/11/2024	Yes	No
Results article	Mixed Methods Analysis	24/06/2025	25/06/2025	Yes	No