

# The Giant PANDA study: which blood pressure medication is best for pregnant women with high blood pressure?

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<b>Registration date</b> 18/11/2020	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 02/10/2025	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Around 10% of women in the UK have high blood pressure in pregnancy, which without treatment can cause serious complications for the woman and baby. We want to find out which of the two most commonly used medicines to treat high blood pressure in pregnancy (labetalol and nifedipine) in the NHS is best at treating high blood pressure without having troublesome side effects for the woman or baby. Both medications have been widely used in the UK for many years and are considered safe in pregnancy.

The study aims to find out which blood pressure medication is best at treating high blood pressure in pregnancy.

Study results will help to understand which medication best treats high blood pressure in pregnancy and is safe for the baby, helping doctors and women with high blood pressure decide which medication is best for each woman and their baby.

### Who can participate?

Pregnant women with hypertension, aged 18 years or over

### What does the study involve?

Over 2,300 pregnant women with high blood pressure from around 50 maternity units in the UK that need treatment for their blood pressure will be offered information about the study and decide if they would like to take part. Women will be asked for their consent to take part and to complete a short questionnaire about how they are feeling. Women will then be randomly allocated (by chance) to either labetalol or nifedipine using a computer. To ensure women are treated safely, women and their healthcare team will know which medication group they are in. All women will continue to have their usual antenatal care including adding and switching their blood pressure medication and changing dose as needed. Two weeks after joining the study women will be asked to complete a few short questionnaires about how they are finding their blood pressure medication. Women and their babies will be followed through the pregnancy until they leave the hospital after birth.

What are the possible benefits and risks of participating?

Taking part will help us to understand how best to treat women with high blood pressure in pregnancy. Because women were about to be prescribed one of these two medications to treat their high blood pressure, there is very little risk to taking part. The only possible disadvantage is the additional time spent with the study team. We will keep these contacts as brief as possible, and if it is easier for women the two-week check-in can be over the phone or by email.

The doctor or healthcare professional prescribing their medication will explain any side effects as they usually would, and they can ask them at any time if they are not sure. The commonest side-effect reported for both drugs in pregnancy is a headache. Some women also reported dizziness or breathlessness. All women will continue to receive their usual NHS care during pregnancy while in this study.

Where is the study run from?

The Birmingham Clinical Trials Unit is running the study with Kings College London (UK)

When is the study starting and how long is it expected to run for?

April 2020 to September 2025

Who is funding the study?

National Institute for Health Research (NIHR) Health Technology Assessment Programme (UK)

Who is the main contact?

Lisa Leighton, Giant-PANDA@trials.bham.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

Mrs Lisa Leighton

### Contact details

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Giant-PANDA@trials.bham.ac.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

2020-003410-12

### Integrated Research Application System (IRAS)

284958

**Protocol serial number**

CPMS 47078, IRAS 284958

## Study information

**Scientific Title**

Pregnancy ANtihypertensive Drugs: which Agent is best?

**Acronym**

Giant PANDA

**Study objectives**

Nifedipine will be superior compared to labetalol with less women in this group with severe systolic blood pressure readings, but the co-primary perinatal outcome will be no worse for the nifedipine group (non-inferior) compared with the labetalol group

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 03/11/2020, London - South East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8085; londonsoutheast.rec@hra.nhs.uk), ref: 20/LO/1110

**Study design**

Interventional randomized controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Oedema, proteinuria and hypertensive disorders in pregnancy, childbirth and the puerperium

**Interventions**

The trial is a pragmatic, open-label, multicentre, two-arm randomised controlled trial of a treatment strategy with nifedipine versus labetalol in women with pregnancy hypertension. We aim to recruit 2,300 pregnant women (less than 34 weeks' gestation), with pregnancy hypertension (chronic or gestational hypertension or pre-eclampsia), over 18 years, able to provide consent and where the decision has been made to initiate or continue use of an antihypertensive drug.

Women will be identified by referral letters and/or at antenatal clinics and approached by a member of the direct clinical care team or the local research team (part of the direct care team) and provided with information on the study and given appropriate time to make the decision to participate. Following informed consent completion, women will be asked to complete a short questionnaire about how they feel. Women will then be randomised, by random allocation (1:1), to treatment with any preparation of modified release nifedipine, a calcium channel blocker,

(intervention arm) or any preparation of labetalol, a mixed alpha/ beta blocker, (active control arm). Two weeks after randomisation women will be contacted by the research team and asked to complete a few short questionnaires about their blood pressure medication. Women and their babies will be in the study from consent until primary hospital discharge or 28 days post birth, whichever occurs sooner.

This study is open-label to ensure women are effectively and safely treated, with healthcare professionals and women aware of their treatment allocation. Dose titration, switching, or add to the randomised antihypertensive drug will occur as in usual clinical practice as clinically indicated throughout pregnancy.

If a woman declines randomisation to the trial then she will be offered participation in the Giant PANDA observational study, involving data collection only. All other aspects of antenatal and delivery care will follow usual clinical care pathways underpinned by NICE 2019 guidelines for pregnancy hypertension.

The starting dose will be left to the discretion of the responsible healthcare professional, guided by blood pressure on the day, previous antihypertensive dose (where applicable) and any other relevant factors. The usual starting dose for the study drugs are:

Labetalol - Oral - 100mg twice a day, increased to a maximum of 2,400mg total daily dose

Nifedipine - Oral - 10mg twice a day, increased to a maximum of 40mg twice daily

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Labetalol, nifedipine

### **Primary outcome(s)**

1. Maternal: Blood pressure measured using a sphygmomanometer daily between randomisation and birth
2. Fetal/neonatal: Composite of fetal loss before birth or known neonatal death, or neonatal unit admission between randomisation up to primary hospital discharge or 28 days post-birth, whichever occurs sooner (with no double counting of outcomes)

### **Key secondary outcome(s)**

Measured using patient records:

Up to birth:

1. Severe hypertension (defined as any episode of severe maternal hypertension (systolic blood pressure  $\geq 160$  mmHg between randomisation and birth))
2. Mean antenatal systolic blood pressure (using highest systolic blood pressure per day as collected for the primary outcome)
3. New diagnosis of pre-eclampsia
4. Severe maternal morbidity (fullPIERS consensus definition (von Dadelszen, Payne et al. 2011))
5. Discontinued allocated antihypertensive drug
6. Undesirable effects of allocated (and other) antihypertensive drug(s) (number of women and number of undesirable effects)

At delivery/birth:

1. Indicated delivery (induction of labour or prelabour rupture of membranes (PROM) with stimulation of labour or pre-labour Caesarean section)

Between birth and primary hospital discharge or 28 days post-birth, whichever occurs sooner:

1. Neonatal unit admission (separation of baby from mother)
2. Major congenital abnormality as defined by EUROCAT
3. Mode of birth (spontaneous vaginal, assisted vaginal, Caesarean section)
4. Gestational age at birth
5. Birthweight centile
6. Need for treatment for neonatal hypoglycaemia (in those having blood glucose monitoring)

### **Completion date**

30/09/2025

## **Eligibility**

### **Key inclusion criteria**

1. Pregnancy 11+0 and 34+6 weeks' gestation inclusive
2. Diagnosis of pregnancy hypertension (chronic/gestational hypertension or pre-eclampsia)
3. Clinician decision to initiate or continue use of antihypertensive drugs
4. Aged 18 years or over
5. Able to give informed consent

For observational study:

6. Women will be eligible to participate in the observational study at any gestational age up to and including 34+6 weeks. Women are able to take part in the observational study prior to 11+0 weeks gestation where the use of any antihypertensive drugs prescribed in clinical care will be recorded but will not form part of the interventional trial

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

Female

### **Total final enrolment**

2254

### **Key exclusion criteria**

1. Contraindication to either labetalol or nifedipine
2. Already taking both labetalol and nifedipine, and not able to be randomised to a single drug

For observational study:

3. Neither exclusion criterion for the trial are relevant for the observational study. Women contraindicated to either labetalol or nifedipine and/or women already taking both labetalol and nifedipine and not able to be randomised to a single drug, are eligible for the observational study

**Date of first enrolment**

08/06/2021

**Date of final enrolment**

17/01/2025

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**St Thomas' Hospital**

Guy's and St Thomas' NHS Foundation Trust

Westminster Bridge Road

London

United Kingdom

SE1 7EH

**Study participating centre**

**Manchester University Hospitals NHS Foundation Trust**

Cobbett House

Oxford Road

Manchester

United Kingdom

M13 9WL

**Study participating centre**

**Liverpool Women's Hospital**

Liverpool Women's NHS Foundation Trust

Crown Street

Liverpool

United Kingdom

L8 7SS

**Study participating centre**

**St James University Hospital**  
Leeds Teaching Hospitals NHS Trust  
Beckett Street  
Leeds  
United Kingdom  
LS9 7TF

**Study participating centre**  
**Leicester Royal Infirmary**  
University Hospitals of Leicester NHS Trust  
Infirmary Square  
Leicester  
United Kingdom  
LE1 5WW

**Study participating centre**  
**Birmingham Women's and Children's NHS Foundation Trust**  
Steelhouse Lane  
Birmingham  
United Kingdom  
B4 6NH

**Study participating centre**  
**Queen's Medical Centre**  
Nottingham University Hospitals NHS Trust  
Derby Road  
Nottingham  
United Kingdom  
NG7 2UH

**Study participating centre**  
**Bristol Royal Infirmary**  
University Hospitals Bristol and Weston NHS Foundation Trust  
Marlborough Street  
Bristol  
United Kingdom  
BS1 3NU

**Study participating centre**  
**Bradford Royal Infirmary**  
Bradford Teaching Hospitals NHS Foundation Trust

Duckworth Lane  
Bradford  
United Kingdom  
BD9 6RJ

**Study participating centre**

**Royal United Hospital**

Combe Park  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**

**Colchester Dist General Hospital**

East Suffolk and North Essex NHS Foundation Trust  
Turner Road  
Colchester  
United Kingdom  
CO4 5JL

**Study participating centre**

**New Cross Hospital**

Royal Wolverhampton NHS Trust  
Wolverhampton Road  
Wolverhampton  
United Kingdom  
WV10 0QP

**Study participating centre**

**Chelsea and Westminster Hospital**

369 Fulham Road  
London  
United Kingdom  
SW10 9NH

**Study participating centre**

**Kingston Hospital NHS Foundation Trust**

Galsworthy Road  
Kingston upon Thames  
United Kingdom  
KT2 7QB

**Study participating centre****St George's Hospital**

St George's University Hospitals NHS Foundation Trust  
Blackshaw Road  
Tooting  
London  
United Kingdom  
ST17 0QT

**Study participating centre****John Radcliffe Hospital**

Oxford University Hospitals NHS Foundation Trust  
Headley Way  
Headington  
Oxford  
United Kingdom  
OX3 9DU

**Study participating centre****Southampton General Hospital**

University Hospital Southampton NHS Foundation Trust  
Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre****Homerton University Hospital NHS Foundation Trust**

Homerton Row  
London  
United Kingdom  
E9 6SR

**Sponsor information****Organisation**

University of Birmingham

ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Government

### Funder Name

NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR128721

### Funder Name

National Institute for Health Research (NIHR) (UK)

### Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### 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. Requests for the final dataset can be made through the chief investigator in accordance with the data-sharing policies of King's College London and Birmingham Clinical Trials Unit, with input from the co-investigator group where applicable.

### IPD sharing plan summary

Available on request

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		12/09/2023	14/09/2023	Yes	No
<a href="#">HRA</a>					

<a href="#">research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Inclusion of people with multiple long-term conditions in pregnancy research: patient, public and stakeholder involvement and engagement in a randomised controlled trial	07/10/2024	08/10/2024	Yes	No
<a href="#">Protocol file</a>	version 1.2	18/08/2023	25/04/2024	No	No
<a href="#">Statistical Analysis Plan</a>	version 1.0		25/04/2024	No	No