Pregnancy ANtihypertensive Drugs: which Agent is best?

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The prize draw was a popular one so we're doing it again!

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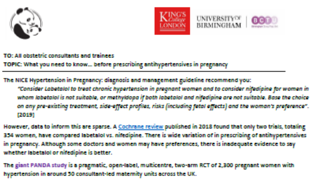
Any healthcare professional who *refers* an eligible woman to your research team in January and February (so you can then offer her the trial) … the referrer will be entered into a prize draw with two opportunities to win a **£50 Cook voucher**

What you need to know…. before prescribing antihypertensives in pregnancy

We have found that the more comfortable doctors and midwives are with the uncertainty around these medications, then the more they are likely to signpost women to the giant PANDA study and the more women feel reassured and are comfortable to commence in the trial. Attached is a memo for all obstetric consultants and trainees and a recent BMJ Uncertainties publication which we would like to share with you. We would be grateful if you could circulate and promote to your consultant and trainee colleagues.



KING'S College LONDON | UNIVERSITY OF BIRMINGHAM | BCTU

TO: All obstetric consultants and trainees
TOPIC: What you need to know… before prescribing antihypertensives in pregnancy

The NICE Hypertension in Pregnancy: diagnosis and management guideline recommend you:

> *"Consider Labetalol to treat chronic hypertension in pregnant women and to consider nifedipine for women in whom labetalol is not suitable, or methyldopa if both labetalol and nifedipine are not suitable. Base the choice on any pre-existing treatment, side-effect profiles, risks (including fetal effects) and the woman's preference".* [2019]

However, data to inform this are sparse. A Cochrane review published in 2018 found that only two trials, totaling 354 women, have compared labetalol vs. nifedipine. There is wide variation of in prescribing of antihypertensives in pregnancy. Although some doctors and women may have preferences, there is inadequate evidence to say whether labetalol or nifedipine is better.

The giant PANDA study is a pragmatic, open-label, multicentre, two-arm RCT of 2,300 pregnant women with hypertension in around 50 consultant-led maternity units across the UK.

PRACTICE

Check for updates

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Additional material is published online only. To view please visit the journal online
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UNCERTAINTIES

Which antihypertensive treatment is better for mild to moderate hypertension in pregnancy?

Danielle Ashworth,[1] Cheryl Battersby,[2] Marcus Green,[3] Pollyanna Hardy,[4] Richard J McManus,[5] Catherine Cluver,[6] Lucy C Chappell[1]

What you need to know

- Pregnancy hypertension (encompassing chronic hypertension, gestational hypertension, and pre-eclampsia) affects around 10% of women
- Labetalol and nifedipine are recommended by national guidelines and commonly used in clinical practice to reduce the risk of developing severe hypertension in these women
- There is little evidence from head-to-head comparisons of effectiveness and tolerability to guide choice of antihypertensive treatment in pregnancy, and uncertainty about impact on clinical outcomes such as stroke, pre-eclampsia, perinatal death, fetal growth restriction, or preterm birth

pregnancy, or due to side effects (methyldopa), or because other drugs within the same class (such as other calcium channel blockers) have better pharmacodynamic profiles but less safety data in pregnancy.

It is uncertain which antihypertensive treatment in pregnancy is associated with optimal maternal and perinatal outcomes. We focus on ongoing antenatal management of mild to moderate pregnancy hypertension (defined as systolic blood pressure 140-169 mm Hg and/or diastolic blood pressure 90-109 mm Hg[1]). Choice of postnatal treatment is not covered here, as drug options are different outside of pregnancy.

BMJ: first published as 10.1136/bmj-2021-066333 on 18 January 2022. Dow

Chronic hypertension
Gestational hypertension
Pre-eclampsia

<35 weeks

We can now make the choice of antihypertensive in pregnancy… *randomized* within the giant PANDA Study, rather than random or arbitrary. This will enable us to give women the information they need to make decisions about their health and pregnancy.

After randomisation:

- You can prescribe the randomised medication as normal (e.g. outpatient prescription, electronic chart, etc.)
- You do not need any involvement of the clinical trials pharmacy and you can use any preparation of modified Release nifedipine or labetalol
- Let the woman know all other aspects of antenatal and delivery care will follow usual clinical care pathways
- Following initial randomization, you can increase, stop, or switch antihypertensive therapy as indicated, in line with your usual practice (and the woman can continue in the trial)

⇨ Please contact the research team in your Trust if you are prescribing (starting OR continuing) antihypertensives in pregnancy before 35 weeks' gestation
⇨ Consider becoming the Associate PI for the giant PANDA study at your maternity unit. More information here
⇨ Receive a certificate for your involvement for portfolio (i.e. referring an eligible woman to the research team)

For more information:

- High blood pressure in pregnancy - infographic
- Which antihypertensive treatment is better for mild to moderate hypertension in pregnancy?
- The giant PANDA study – Professor Lucy Chappell

Around 18 million women have pregnancy hypertension each year, with approximately 27 800 maternal deaths as per 2019 Global Burden of Disease estimates. In the UK, approximately 8-10% of pregnant women (around 70 000 each year) have high blood pressure in pregnancy (also known as pregnancy hypertension).[1] This includes chronic hypertension, gestational hypertension, and pre-eclampsia (fig 1). Age standardised incidence rates are highest in sub-Saharan African countries.[2]

Pregnancy hypertension is associated with adverse maternal and perinatal outcomes.[3 4] These may be related to direct complications such as maternal stroke, pregnancy-specific disorders such as pre-eclampsia, and fetal growth restriction, often mediated through impaired placental function. These conditions may affect the infant through iatrogenic preterm delivery or perinatal death.

International guidelines recommend pharmacological treatment for pregnancy hypertension. Blood pressure thresholds for initiating treatment differ (table 1). The most widely recommended antihypertensive drugs in pregnancy are:

- Labetalol—a mixed α and β blocker administered orally or intravenously
- Nifedipine—an oral calcium channel blocker
- Methyldopa—an oral antiadrenergic agent.

Antihypertensive therapies are applied similarly across chronic hypertension, gestational hypertension, and pre-eclampsia in most settings. These antihypertensives are not commonly used outside of pregnancy, because there are more effective drug classes (such as renin-angiotensin system blockers) that are contraindicated in

Chronic hypertension
Blood pressure ≥140/90 mm Hg
Pre-pregnancy or present <20 weeks of pregnancy
Gestational hypertension
Blood pressure ≥140/90 mm Hg
First present ≥20 weeks of pregnancy
Pre-eclampsia or superimposed pre-eclampsia (on chronic hypertension)
Chronic hypertension
OR
Gestational hypertension
AND one or more of the below features
Proteinuria
Renal dysfunction (e.g. acute kidney injury)
Hepatic dysfunction (e.g. raised transaminases)
Haematological dysfunction (e.g. thrombocytopenia)
Neurological features (e.g. eclampsia)
Cardiorespiratory dysfunction (e.g. pulmonary oedema)
Uteroplacental dysfunction (e.g. fetal growth restriction)

Fig 1 | Types of hypertension in pregnancy

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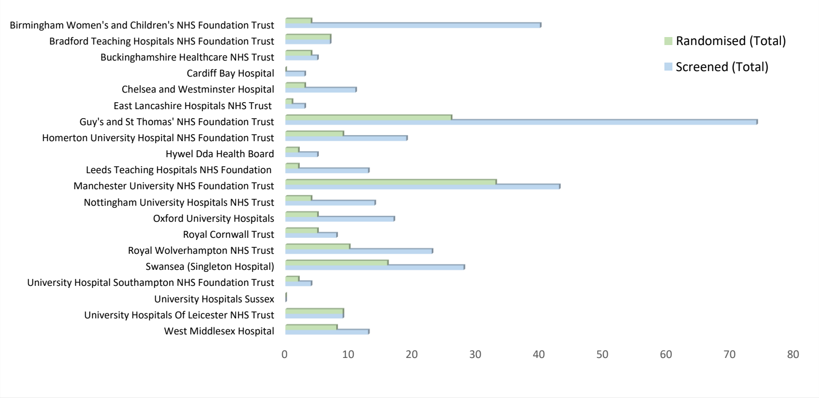
Study update – February 2022

- 21 Trusts (22 sites) now open
- 37 participants randomised in January

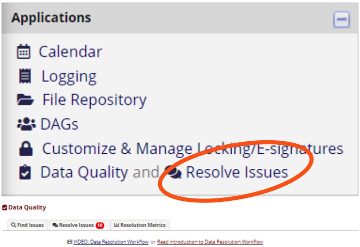
	Date opened	Screened (Total)	Randomised (Total)	Randomised (Jan 2022)	Latest randomisation
Birmingham Women's and Children's NHS Foundation Trust	26-05-21	40	4	**0**	**30-09-21**
Bradford Teaching Hospitals NHS Foundation Trust	25-08-21	7	7	**0**	**31-12-21**
Buckinghamshire Healthcare NHS Trust	30-09-21	6	4	**0**	**16-12-21**
Cardiff Bay Hospital	09-11-21	5	1	**1**	**06-01-22**
Chelsea and Westminster Hospital	21-07-21	15	7	**4**	**26-01-22**
East Lancashire Hospitals NHS Trust	29-09-21	5	3	**2**	**17-01-22**
East Suffolk and North Essex NHS Foundation Trust - Ipswich	14-12-21	2	0	**0**	**n/a**
Guy's and St Thomas' NHS Foundation Trust	16-06-21	79	30	**4**	**29-12-21**
Homerton University Hospital NHS Foundation Trust	11-06-21	26	9	**0**	**05-11-21**
Hywel Dda Health Board	09-11-21	7	3	**1**	**05-01-22**
Leeds Teaching Hospitals NHS Foundation	22-09-21	18	4	**2**	**21-01-22**
Manchester University NHS Foundation Trust	05-10-21	57	45	**12**	**28-01-22**
Nottingham University Hospitals NHS Trust	27-07-21	16	6	**2**	**28-01-22**
Oxford University Hospitals	10-09-21	19	6	**1**	**18-01-22**
Royal Cornwall Trust	10-08-21	9	5	**0**	**02-12-21**
Royal Wolverhampton NHS Trust	14-06-21	28	10	**0**	**22-11-21**
Sheffield Teaching Hospitals NHS Foundation Trust	20-01-22	1	1	**1**	**28-01-22**
Swansea (Singleton Hospital)	26-05-21	34	20	**4**	**27-01-22**
University Hospital Southampton NHS Foundation Trust	19-07-21	4	2	**0**	**01-12-21**
University Hospitals Sussex	16-11-21	1	0	**0**	**n/a**
University Hospitals Of Leicester NHS Trust	14-07-21	9	9	**0**	**02-12-21**
West Middlesex Hospital	21-07-21	18	11	**3**	**20-01-22**
Grand Total		**406**	**187**	**37**	



Tips to find eligible women:

- Screen booking – ask your clerks/ community midwives to call / email you when they have someone with hypertension
- Screen clinic lists (e.g. maternal medicine, diabetes, renal, hypertension, etc.)
- Check in daily with antenatal clinic, MAU/DAU, antenatal ward and labour ward. Keep reminding them to email/ call you.
- Present at your clinical governance / MDT meetings to raise awareness of the trial
- Email the criteria for the trial to your doctors and midwives (https://www.youtube.com/watch?v=S1sTQmKKiJI)
- Keep reminding doctor and midwives to call when they are writing an antihypertensive prescription – key cards, quick reference leaflets on antenatal clinic desks
- Posters in staff and patient areas
- Stickers on outpatient prescription drawer
- Patient information leaflets in home blood pressure service package
- Get an Associate PI! https://www.nihr.ac.uk/health-and-care-professionals/career-development/associate-principal-investigator-scheme.htm

Have you responded to your data queries on REDCap?

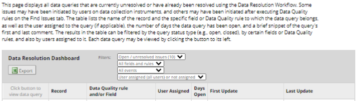

Applications
Calendar
Logging
File Repository
DAGs
Customize & Manage Locking/E-signatures
Data Quality and Resolve Issues
Data Quality
Find Issues
Resolve Issues 10
Resolution Metrics
VIDEO: Data Resolution Workflow or Read introduction to Data Resolution Workflow

1. Login to REDCap

2. Click on 'Resolve Issues' (bottom left-hand side) which will list all queries

3. You can see the query and any updated response according to participant id

4. Please update eCRF (if applicable) and respond to the query to say what you have done (for audit



This page displays all data queries that are currently unresolved or have already been resolved using the Data Resolution Workflow. Some issues may have been initiated by users on data collection instruments, and others may have been initiated after executing Data Quality rules on the Find Issues tab. The table lists the name of the record and the specific field or Data Quality rule to which the data query belongs, as well as the user assigned to the query (if applicable), the number of days the data query has been open, and a brief snippet of the query's first and last comment. The results in the table can be filtered by the query status type (e.g., open, closed), by certain fields or Data Quality rules, and also by users assigned to it. Each data query may be viewed by clicking the button to its left.

Data Resolution Dashboard

Filters: Open / unresolved issues (10); All fields and rules; All events; User assigned (all users) or not assigned

Click button to view data query	Record	Data Quality rule and/or Field	User Assigned	Days Open	First Update	Last Update

trail)

5. Set aside a time to check back regularly (monthly) for new queries

Contact the team

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