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What causes high blood pressure in young people: the heart or blood vessels?

Submission date 25/07/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 09/08/2023	**Overall study status** Ongoing	
Last Edited 07/08/2026	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Around a third of the adult population suffers from high blood pressure (medically known as “hypertension”). If left untreated, hypertension is a major risk factor for having a heart attack or a stroke. More and more children are being diagnosed with high blood pressure with no obvious cause. This is partly because doctors are checking for it more, but also because it is a common problem that develops alongside being overweight. Not much is known about what causes hypertension in children. This research aims to address this gap by looking in detail at a group of hypertensive children and young adults and comparing them to a group with normal blood pressure. The study will use state-of-the-art blood pressure measurements and heart scans to measure the flow of blood in the heart and blood vessels of participants. The study will also manipulate some of the messages getting from the brain to control the heart and blood vessels and measure the effect of these.

Who can participate?
Children and young adults with primary hypertension aged 10 to 35 years old and under the care of specialist teams at St Thomas’ Hospital and Evelina London Children’s Hospital. Children and young adults who are healthy with normal weight and normal blood pressure aged 10 to 35 years old.

What does the study involve?
The study involves having two different types of heart scan: an echocardiogram and an MRI scan, plus some detailed blood pressure measurements which will also measure arterial stiffness. The arterial stiffness measurements will be repeated after having some cuffs on the legs inflated to a low pressure for 3-5 minutes and also after doing a slow breathing exercise for about 15 minutes. The team will also collect blood and urine samples (optional for healthy participants).

Some of the participants with high blood pressure will be asked to return for a repeat set of measurements if their blood pressure reduces over time.

What are the possible benefits and risks of participating?
There are no direct benefits to you from taking part. You will be contributing to research that will improve understanding of high blood pressure which may benefit people of all ages with high blood pressure in the future.

There are no serious risks we anticipate in this study. The main drawbacks of taking part are the extra time and inconvenience for you to visit the hospital for the research study and the discomfort you may experience in the MRI scanner and having a blood test.

Where is the study run from?
St Thomas' Hospital (UK)

When is the study starting and how long is it expected to run for?
March 2022 to February 2028

Who is funding the study?
1. The Medical Research Council (MRC) (UK)
2. The British Heart Foundation (UK)

Who is the main contact?
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Contact information

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Additional identifiers

Integrated Research Application System (IRAS)
306122

Central Portfolio Management System (CPMS)
55164

Study information

Scientific Title
Haemodynamic determinants of hYpertension in Children and Young People and role of the sympathetic nervous system: HY CYP

Acronym
HY CYP

Study objectives
Current study objectives as of 07/08/2026:
The study aims to test if primary hypertension in children and young people results

predominantly from cardiac overactivity (increased heart rate, cardiac output and aortic ejection velocity) and a secondary increase in proximal aortic stiffening rather than an increase in systemic vascular resistance. Cardiac overactivity activity in primary hypertension may result from increased sympathetic nervous system activity, mediated through β-adrenergic receptors acting to increase heart rate, stroke volume, cardiac output and aortic ejection velocity.

In addition, children and young people with primary hypertension have stiffer arteries than healthy subjects of the same age without hypertension. The study aims to investigate if this is due to increased mean arterial pressure or increased sympathetic nervous system activity.

Previous study objectives:
Primary hypertension in children results predominantly from cardiac overactivity (increased heart rate, cardiac output and aortic ejection velocity) and a secondary increase in proximal aortic stiffening rather than an increase in systemic vascular resistance.

Cardiac overactivity activity in primary hypertension results from increased sympathetic nervous system activity, mediated through β-adrenergic receptors acting to increase heart rate, stroke volume, cardiac output and aortic ejection velocity.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 27/06/2023, South Birmingham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None available; Southbirmingham.rec@hra.nhs.uk), ref: 23/WM/0122

2. Approved 15/04/2025, South Birmingham Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None available; Southbirmingham.rec@hra.nhs.uk), ref: 23/WM/0122

Primary study design
Observational

Study design
Observational cohort study (study 1) with an interventional substudy (study 2)

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Paediatrics and cardiology

Interventions
Current methodology as of 07/08/2026:
PARTICIPANTS
Children and young adults with primary hypertension aged 10-35 years will be approached by a member of their direct clinical care team. We aim to recruit 75 patients, 50% under 18 years and 50% 18-35 years, with 50% female. Participants should not be on medication (i.e., are managing their hypertension with lifestyle modification measures). If they are on medication, they need to be able to stop their medication for a 2-week washout period before the study and stay off their

medication until the collection of all data (up to 2 months), in the opinion of their lead clinician. For Study 2, we will seek to recruit 20 hypertensive patients from the original Study 1 cohort, at the point at which they will be commencing antihypertensive medication for clinical reasons.

50 control participants aged 10-35 years will be recruited from existing databases of healthy controls. These participants have previously participated in clinical studies with our group and have consented to be contacted about further studies in the future. We aim to recruit 50 patients, 50% under 18 years and 50% 18-35 years, with 50% female. They will need to be of normal blood pressure and healthy weight, i.e., not overweight, or obese. Another 25 control participants will be consented prospectively to ensure adequate recruitment to all sub-tests in the study.

STUDY 1 (all participants)
Data to be collected is as follows, with no specific order necessary:
1. Height, weight, BMI, and measures of adiposity. Pubertal status for those who have not yet completed puberty.
2. Standardised depression and anxiety questionnaire
3. Blood test: kidney function, measures of sympathetic nervous system activity, measures of heart function, metabolic markers
4. Urine test: sodium (salt) levels, measures of sympathetic nervous system activity
5. Cardiac MRI: 40-minute MRI scan of the heart with blood pressure measured before and after the scan
6. Blood pressure, heart rate variability and arterial stiffness measurements: these are non-invasive and require inflation of a blood pressure cuff, placement of electrode (ECG) stickers on the chest and/or limbs and placing a probe over the pulse points in the neck, groin and wrist respectively.
7. Echocardiogram: a 30-minute ultrasound scan of the heart. This is clinically indicated for all hypertensive participants however some more detailed images will be captured for research, lengthening the scan by 10 minutes.
8. Device-guided breathing: participants will be asked to listen to an audio track which helps them slow their breathing. This has the effect of inhibiting the sympathetic nervous system and lowering blood pressure. Limited echocardiogram and haemodynamic measurements as listed in (6) will be performed. This is likely to take 10-20 minutes depending on how long each participant takes to achieve a steady state with their breathing.
9. Leg venous occlusion: Pneumatic cuffs are placed around the thighs and inflated to a low pressure for 3 minutes, causing a gentle accumulation of fluid in the legs but without any swelling. Arterial stiffness measurements are repeated after this time

We anticipate that all investigations in Study 1 may be completed in two visits, at least one of which could be on the same day as a clinical visit.

There is an optional sub-study which participants may also choose to participate in:
Optional Study 1A:
1. Aortic ultrasound: Two ultrasound probes will be used to measure flows in the aorta at two points in the chest simultaneously. These measurements will be performed at rest and whilst the subject performs guided breathing exercises. This will give an estimate of aortic stiffness. All subjects, whether normotensive or hypertensive may participate in this test.
2. Clonidine test: A modified clonidine suppression test will be used to examine effects of a reduction in sympathetic activity on arterial stiffness. This test will only be offered to subjects with confirmed hypertension.

STUDY 2 (a subgroup of 20 hypertensive participants):
1. Administration of antihypertensive agent 1 (bisoprolol): participants will take this medication for 10-14 days at a clinically effective dose. A limited echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes.
2. Administration of antihypertensive agent 2 (amlodipine): participants will take this medication for 10-14 days at a clinically effective dose. Echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes. The order in which participants receive antihypertensive agents 1 and 2 will be randomised.

Previous methodology:
PARTICIPANTS
Children and young adults with primary hypertension aged 10-35 years will be approached by a member of their direct clinical care team. We aim to recruit 50 patients, 50% under 18 years and 50% 18-35 years, with 50% female. Participants should not be on medication (i.e., are managing their hypertension with lifestyle modification measures). If they are on medication, they need to be able to stop their medication for a 2-week washout period before the study and stay off their medication until the collection of all data (up to 2 months), in the opinion of their lead clinician. For Study 2, we will seek to recruit 20 hypertensive patients from the original Study 1 cohort, at the point at which they will be commencing antihypertensive medication for clinical reasons.

50 control participants aged 10-35 years will be recruited from existing databases of healthy controls. These participants have previously participated in clinical studies with our group and have consented to be contacted about further studies in the future. We aim to recruit 50 patients, 50% under 18 years and 50% 18-35 years, with 50% female. They will need to be of normal blood pressure and healthy weight, i.e., not overweight, or obese.

STUDY 1 (all 100 participants)
Data to be collected is as follows, with no specific order necessary:
1. Height, weight, BMI, and measures of adiposity. Pubertal status for those who have not yet completed puberty.
2. Standardised depression and anxiety questionnaire
3. Blood test: kidney function, measures of sympathetic nervous system activity, measures of heart function, metabolic markers
4. Urine test: sodium (salt) levels, measures of sympathetic nervous system activity
5. Cardiac MRI: 40-minute MRI scan of the heart with blood pressure measured before and after the scan
6. Blood pressure, heart rate variability and arterial applanation tonometry measurements: these are non-invasive and require inflation of a blood pressure cuff, placement of electrode (ECG) stickers on the chest and/or limbs and placing a probe over the pulse points in the neck, groin and wrist respectively.
7. Echocardiogram: a 30-minute ultrasound scan of the heart. This is clinically indicated for all hypertensive participants however some more detailed images will be captured for research, lengthening the scan by 10 minutes.
8. Device-guided breathing: participants will be asked to listen to an audio track which helps them slow their breathing. This has the effect of inhibiting the sympathetic nervous system and lowering blood pressure. Limited echocardiogram and haemodynamic measurements as listed in (6) will be performed. This is likely to take 10-20 minutes depending on how long each participant takes to achieve a steady state with their breathing.

We anticipate that all investigations in Study 1 may be completed in two visits, at least one of which could be on the same day as a clinical visit.

STUDY 2 (a subgroup of 20 hypertensive participants):
1. Administration of antihypertensive agent 1 (bisoprolol): participants will take this medication for 10-14 days at a clinically effective dose. A limited echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes.
2. Administration of antihypertensive agent 2 (amlodipine): participants will take this medication for 10-14 days at a clinically effective dose. Echocardiogram and haemodynamic measurements as listed above in (6) will be performed. This visit will take 15-30 minutes. The order in which participants receive antihypertensive agents 1 and 2 will be randomised.

Intervention Type
Mixed

Primary outcome(s)
Current primary outcomes as of 07/08/2026:
1. Cardiac output measured MRI at baseline in hypertensive participants compared to healthy controls
2. Aortic ejection velocity measured using MRI at baseline in hypertensive participants compared to controls
3. Arterial stiffness in hypertensive participants compared to healthy controls, measured using MRI and carotid-femoral pulse wave velocity at baseline
4. Reduction in arterial stiffness in hypertensive subjects after therapeutic reduction in blood pressure, measured using MRI and carotid-femoral pulse wave velocity at baseline and when adequate blood pressure reduction is achieved (duration of time required to achieve this may be variable)

Previous primary outcomes:
1. Cardiac output measured MRI at baseline in hypertensive participants compared to healthy controls
2. Aortic ejection velocity measured using MRI at baseline in hypertensive participants compared to controls

Key secondary outcome(s)
Current secondary outcomes as of 07/08/2026:
1. Cardiac output measured using an echocardiogram before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
2. Aortic ejection velocity measured using echocardiogram before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
3. Pulse wave velocity measured using applanation tonometry before and after i) slow breathing exercise, ii) leg venous occlusion, iii) amlodipine administration and iv) bisoprolol administration
4. Systemic vascular resistance, heart rate, stroke volume and pulse wave velocity measured using MRI at baseline in hypertensive participants compared to controls
5. Changes in aortic stiffness after acute change in thoracic pressure with breathing manoeuvres in hypertensive subjects compared to controls, measured using aortic pulse wave velocity at study baseline in healthy controls, or at baseline and/or at time of adequate blood pressure reduction for hypertensive subjects (duration of time required to achieve this may be variable)

Previous secondary outcomes:
1. Cardiac output measured using an echocardiogram before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
2. Aortic ejection velocity measured using echocardiogram before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration

3. Pulse wave velocity measured using applanation tonometry before and after i) slow breathing exercise, ii) amlodipine administration and iii) bisoprolol administration
4. Systemic vascular resistance, heart rate, stroke volume and pulse wave velocity measured using MRI at baseline in hypertensive participants compared to controls

Completion date
29/02/2028

Eligibility

Key inclusion criteria
1. Aged 10-35 years old
2. Primary hypertension (intervention group) or BP < 90th centile (control group)
3. Able to tolerate the planned investigations
4. Not currently on anti-hypertensive medication/s or able to stop anti-hypertensive medications for 2 weeks prior to any research-related assessments.

Additional inclusion criteria control participants:
5. BMI in the "normal" range for age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
10 Years

Upper age limit
35 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Secondary hypertension
2. Clinical urgency to commence anti-hypertensive or unable to stop anti-antihypertensives for 2 week washout period
3. Unable to obtain adequate quality of planned cardiovascular investigations
4. Congenital heart disease
5. Cardiac dysrhythmias
6. Pregnancy or lactating mothers

Additional exclusion criteria for medication 1 (bisoprolol challenge):
7. Asthma currently treated with medication
8. Cardiac conduction abnormalities
9. Known intolerance to bisoprolol

Additional exclusion criteria for medication 2 (amlodipine challenge):
10. History of angina or myocardial infarction
11. Known intolerance to amlodipine

Date of first enrolment
01/09/2023

Date of final enrolment
31/01/2028

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
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Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
British Heart Foundation

Alternative Name(s)
The British Heart Foundation, the_bhf, BHF

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
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Manish Sinha, manish.sinha@gstt.nhs.uk. These datasets include haemodynamic baseline data from echocardiograms and cardiac MRI, available from approximately September 2027, patients will be consented for sharing of anonymised data.

IPD sharing plan summary
Available on request