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# Using health information and blood tests (metabolites) to personalise the treatment of high blood pressure

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| **Submission date**<br>04/09/2025 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>18/12/2025 | **Overall study status**<br>Ongoing | |
| **Last Edited**<br>17/07/2026 | **Condition category**<br>Circulatory System | |

## Plain English summary of protocol

Background and study aims
High blood pressure (hypertension) affects around one in three adults and can cause serious health problems such as a stroke or heart attack. Medication to lower blood pressure is proven to reduce the risk of these complications. There are many different drugs that can treat high blood pressure, and a combination of tablets at lower dose is usually the best option. However, choosing the right combination for each person is difficult, which can lead to side effects or poor control of blood pressure.
The HYPERMARKER trial has been developed with the support of a Patient and Public Involvement Team. It is testing whether providing doctors with additional information when they decide on which medication to prescribe can improve a patient's overall blood pressure management. This includes relevant medical information and personalised results from blood tests, brought together using computer programs (machine learning) – a 'smart approach'. The blood tests check for small substances naturally produced by the body called metabolites. These might indicate how a patient might react to certain medications.

Who can participate?
Adults (aged 18 years and over) with a recent high blood pressure reading (systolic blood pressure ≥140 mmHg) that needs treatment with tablets

What does the study involve?
Potential participants must first confirm they are happy to take part by signing a consent form. After signing the form, the team will collect information about participants medication and medical history, take measurements including weight and blood pressure, and collect a blood sample (for the metabolite test). Participants will then complete a questionnaire about their diet over the last 24 hours. Participants will then be provided with, and trained to use a blood pressure machine and the studies mobile app. This will be used throughout the study to keep a record of participants blood pressure measurements so these can all be done from home. Each participant will initially complete 1 week of home blood pressure recordings. A week of readings should consist of at least two blood pressure readings morning and evening for 3 days. Participants will also be sent baseline socioeconomic and demographic, quality of life and

healthcare utilisation questionnaires to complete at baseline.
Each participant will be assigned randomly to one of two groups (A or B) to test and improve the new smart approach. Everyone will have their medications reviewed and if needed, changed by the healthcare team; those in Group A will first receive medication as per normal routine practice (standard of care; without any additional information). Those in Group B will have medication prescribed by a doctor with access to the extra information from the smart approach. All participants will then be asked to monitor their blood pressure for 4 weeks. They will also be asked to complete a set of study questionnaires. The questionnaires can be completed at home using an electronic device (smartphone, tablet or computer) and assess participants views on their own health, how they are finding the treatment, and their use of healthcare services.
After the initial 4 weeks, all participants will have their medication re-reviewed by a doctor which may lead to a change in their tablets. This time all participants healthcare teams will have access to the extra information from the smart approach which will be updated throughout the trial. They will then be asked to check their blood pressure again for 4 weeks and complete a further set of questionnaires.
The main outcome of the trial is home systolic blood pressure recordings comparing the standard of care approach and the new smart approach. The study is expected to take 9-16 weeks for each participant to complete.

What are the possible benefits and risks of participating?
Clinical research is important to advance how we manage patients in the future. The information from the study, may help the research team to improve how doctors treat high blood pressure. Participants may also directly benefit via receipt of blood pressure monitor and connected mobile app to use at home during the study. This may help participants and the team better track their blood pressure to make sure it stays under control. The study will also use special blood tests that are not currently available in routine healthcare.
Taking part in the study will involve having at least one blood test, which some people may find a little uncomfortable and may cause temporary bruising or swelling afterwards. Participants medications are likely to be changed during the study, whilst changes take effect, this could cause fluctuation in their blood pressure.

Where is the study run from?
The study is sponsored by the University of Birmingham (UK). The HYPERMARKER research group is led by the University Medical Center Utrecht (the Netherlands). The study plans to recruit patients from four hospital sites across Europe: INCLIVA Instituto de Investigación Sanitaria, Válencia, Spain; University Hospitals Birmingham NHS Foundation Trust, Birmingham, England; University Medical Center Hamburg-Eppendorf, Hamburg, Germany; and University Medical Center Utrecht, Utrecht, the Netherlands.

When is the study starting and how long is it expected to run for?
The study is expected to start in March 2026 pending all appropriate approvals and be completed by December 2026.

Who is funding the study?
The study is funded by the European Union and UK Research and Innovation.

Who is the main contact?
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# Additional identifiers

### Integrated Research Application System (IRAS)
354889

### Central Portfolio Management System (CPMS)
68255

### Protocol serial number
RG_24-123

# Study information

### Scientific Title
Personalised pharmacometabolomic-guided strategy trial to optimise treatment for hypertension (HYPERMARKER)

### Acronym
HYPERMARKER

### Study objectives
Primary Objectives:
1. Determine the effect of using specialist blood tests looking at small substances naturally produced by the body (metabolites) - a pharmacometabolomic-guided drug class approach to guide hypertension treatment on home systolic blood pressure, compared to standard of care.
2. Develop, test and iterate a strategy to support personalised decision-making for hypertension treatment, including active participation from empowered patients.

Secondary Objectives:
1. Compare the proportion of participants achieving a target home SBP of 120–129mmHg with a pharmacometabolomic approach versus standard of care.
2. Compare the incidence of treatment-related adverse effects with a pharmacometabolomic approach versus standard of care.
3. Compare treatment withdrawal due to patient-reported adverse events or adverse reactions with a pharmacometabolomic approach versus standard of care.
4. Compare patient-reported adherence to antihypertensive treatment with a pharmacometabolomic approach versus standard of care.
5. Evaluate the rate of change in home SBP following new therapy, comparing a pharmacometabolomic approach with standard of care.
6. Compare home diastolic blood pressure with a pharmacometabolomic approach versus standard of care.
7. Determine the effect of an iterated and updated pharmacometabolomic approach on home SBP.
8. Determine the effect of an iterated and updated pharmacometabolomic approach on

treatment-related adverse effects.
9. Compare the incidence of serious adverse events with any pharmacometabolomic approach versus standard of care.
10. Compare the incidence of healthcare utilisation events with any pharmacometabolomic approach versus standard of care.
11. Identify changes in patient-reported quality of life across the different treatment phases of the trial.
12. Explore changes in metabolomic profile after hypertension treatment, stratified by drug class.
13. Explore how dietary intake impacts on metabolomic profiles and blood pressure response to antihypertensive treatment.
14. Conduct a cost-utility analysis using cost and quality of life (EQ-5D-5L) to derive a cost per Quality-Adjusted Life year (QALY) gained comparing the pharmacometabolomic approach with standard of care.
15. Conduct a benefit analysis expressing the net monetary benefits/costs of the intervention in the trial setting comparing the pharmacometabolomic approach with standard of care.
16. Develop a probabilistic decision analytical model comprising of (1) a decision tree that captures the short-term clinical outcomes and costs associated with the two arms of the RCT in phase one, with a time horizon defined by the duration of the trial follow-up (12 weeks).
17. Using process mapping methods, map clinical sequelae and resource utilisation across various pathways of care in the European healthcare setting.
18. Conduct time-driven activity-based costing across pathway models and identify and rank cost drivers.

## Ethics approval required
Ethics approval required

## Ethics approval(s)
Approved 03/11/2025, North West – Greater Manchester West Research Ethics Committee (2 Redman Place Stratford, London, E20 1JQ, United Kingdom; -; Gmwest.rec@hra.nhs.uk), ref: 25 /NW/0296

## Primary study design
Interventional

## Study design
Proof-of-concept pragmatic adaptive open-label strategy trial embedded in routine clinical practice with stratified individual patient randomization

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Hypertension

## Interventions
The trial is organised into two phases. In the first phase, participants will be randomised to usual standard of care (group A) for treatment selection, or initial pharmacometabolomic approach (group B). Randomisation will be stratified by site (four sites), participant age (18-69 and ≥70 years), and baseline SBP (SBP 140-159mmHg or ≥160 mmHg), allocating the participants 1:1 to either Group A or Group B In the second phase, participants originally randomised to group A

will have their medications re-reviewed by the clinical investigator with access to the latest iteration of the pharmacometabolomic approach. Similarly, those originally randomised to group B will also potentially benefit from updates to the pharmacometabolomic approach during the course of the trial.

Intervention (Pharmacometabolomic approach):
The intervention will combine metabolomic and clinical data using machine learning to provide additional information clinical investigators may utilise in their choice of blood pressure-lowering medication class for individual patients (pharmacometabolomic approach). To allow for an improved approach in the second phase of the trial, the pharmacometabolomic approach will be iterated and refined during the trial as additional metabolomic and clinical data are obtained.

Control (Standard of care):
Standard of care for this trial is defined according to the 2024 European Society of Cardiology Guidelines for the management of elevated blood pressure and hypertension.

## Intervention Type
Other

## Primary outcome(s)
Change in home systolic blood pressure (SBP) will be derived from all available patient-measured SBP recordings, comparing the intervention and standard of care groups at the end of the first phase of the trial. This includes 1-week of monitoring after enrolment (anticipated minimum of 12 recordings) and at least 4- weeks of monitoring after therapy change (anticipated minimum of 48 recordings).

## Key secondary outcome(s)
The following secondary outcomes will compare the pharmacometabolomic-guided drug class approach and standard of care groups at the end of the first phase of the trial:
1. Proportion of participants achieving a target home systolic blood pressure (SBP) of 120–129 mmHg using the average of the final 3 days of at-home blood pressure measurements from week 4 post intervention.
2. Proportion of participants reporting any treatment-related adverse effects compiled from the Summary of Product Characteristics from the different classes of anti-hypertensive medications. Adverse effects are measured using the patient reported adherence questionnaire sent at week 4 post intervention.
3. Proportion of participants reporting withdrawal of an anti-hypertensive medication. Withdrawal is measured using the patient reported adherence questionnaire sent at week 4 post intervention with a recall timeframe of two weeks.
4. Proportion of participants reporting ≥90% adherence to prescribed anti-hypertensive medication. Adherence is measured using the patient reported adherence questionnaire sent at week 4 post intervention with a recall timeframe of 10 days.
5. Rate of change in home SBP measured using all at-home blood pressure measurements averaged per week.
6. Change in home diastolic blood pressure derived from all available at-home blood pressure measurements.

The following secondary outcomes will separately compare the original intervention, updated intervention and standard of care groups at the end of the second phase of the trial:
7. Change in home SBP using all available SBP measurements, comparing the iterated pharmacometabolomic approach versus the initial pharmacometabolomic approach, and the

iterated pharmacometabolomic approach versus initial standard of care.
8. Patient-reported treatment-related side effects, comparing the iterated pharmacometabolomic approach versus the initial pharmacometabolomic approach, and the iterated pharmacometabolomic approach versus initial standard of care. Sides effects are measured using the patient reported adherence questionnaire sent at week 4 post each intervention.

The following outcomes will apply across the phases of the trial comparing any pharmacometabolomic approach versus standard of care:
9. Proportion and number of serious adverse events (SAEs), including all-cause hospitalisation and death. SAEs are measured through investigator case report forms which may be completed throughout the duration of the trial.
10. Proportion and number of healthcare utilisation events, including details on hospitalisation (frequency, cause, type [outpatient, emergency, admission] and length of stay) and primary care interaction (frequency, cause and type [doctor, nurse, other allied health professional]). Healthcare utilisation events are measured through a patient reported healthcare utilisation questionnaire completed at baseline and week 4 of each intervention phase.
11. Patient-reported quality of life measured using the EuroQol EQ-5D-5L summary index score and visual analogue scale. EQ-5D-5L questionnaires are completed at baseline and at week 4 of each intervention phase.

The following outcomes are unrelated to the randomised group:
12. Change in metabolomic profile, measured from baseline to (optional) follow-up blood sample at the end of trial and stratified by class of anti-hypertensive medication (exploratory).
13. Association between dietary intake, metabolomic profile and blood pressure response to prescribed antihypertensive treatment (exploratory). Dietary intake is measured using validated dietary questionnaires (myfood24 and Compl-eat) completed at baseline and optionally at the end of trial.

Health economic outcomes:
14. Life years and quality-adjusted life years (QALYs) gained
15. Net monetary benefits of the pharmacometabolomic approach
16. Difference in healthcare utilisation and cost estimates between standard care and the pharmacometabolomic approach

### Completion date
30/12/2026

# Eligibility

### Key inclusion criteria
1. Systolic blood pressure ≥140 mmHg on any blood pressure recording method (office, home or ambulatory)
2. Age 18 years or older
3. Clinical indication for antihypertensive therapy

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Mixed

### Lower age limit
18 Years

### Upper age limit
100 Years

### Sex
All

### Total final enrolment
0

### Key exclusion criteria
1. Systolic blood pressure ≥180 mmHg on any blood pressure recording method (office, home or ambulatory)
2. Potential secondary cause of hypertension, including but not limited to renovascular hypertension, endocrine conditions, chronic kidney disease, coarctation of the aorta or medication related.
3. Three or more current anti-hypertensive medications
4. Planned intervention for hypertension, such as renal denervation
5. Severe kidney disease (estimated glomerular filtration rate <30 mL/min)
6. Diagnosis of known heart failure with left ventricular ejection fraction <40%
7. Stroke or myocardial infarction within the last 6 months
8. Pregnancy, planning for pregnancy, or breastfeeding
9. Participant whom the Clinical Investigator deems otherwise ineligible

### Date of first enrolment
09/03/2026

### Date of final enrolment
01/10/2026

## Locations

### Countries of recruitment
United Kingdom

England

Germany

Netherlands

Spain

**Study participating centre**
**University Hospitals Birmingham NHS Foundation Trust**
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# Sponsor information

**Organisation**
University of Birmingham

**ROR**
https://ror.org/03angcq70

# Funder(s)

**Funder type**
Government

**Funder Name**
HORIZON EUROPE European Research Council

**Alternative Name(s)**
European Research Council, Horizon Europe - European Research Council, EU - Horizon Europe - ERC, European Research Council (ERC), Conseil européen de la recherche, Consejo Europeo de Investigación, Det Europæiske Forskningsråd, Europäischer Forschungsrat, ERC, CER, CEI, EFR

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**

**Funder Name**
UK Research and Innovation

**Alternative Name(s)**
UKRI

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**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? |
|---|---|---|---|---|---|
| Protocol article | | 16/07/2026 | 17/07/2026 | Yes | No |
| Study website | | 11/11/2025 | 11/11/2025 | No | Yes |