ISRCTN18030225 https://doi.org/10.1186/ISRCTN18030225

Optimising prescription of treatment in older patients with mild hypertension (high blood pressure) at increased risk of serious adverse events

Submission date
03/02/2023

Recruitment status
No longer recruiting

Registration date
19/09/2023

Overall study status
Ongoing

Last Edited
04/12/2025

Condition category
Circulatory System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The population of the UK is getting older and more people are living with multiple illnesses, taking lots of tablets to manage these illnesses. High blood pressure is one of the most common medical conditions in older people and many take two or more drugs to treat it.

Recent scientific studies suggest that large reductions in blood pressure, and too many drug prescriptions, may be associated with an increase in falls and death in older patients. We have previously undertaken a trial which showed that reducing the number of blood pressure lowering drugs prescribed to older people is safe in the short term (over a 3-month period). However, we do not know what the longer term effects of stopping blood pressure lowering drugs are. This trial aims to assess this in people aged 75 years or older, who have blood pressure in a normal range, are taking two or more medications and are at a higher risk of drug-related side-effects.

This trial will establish whether deprescribing common drugs that lower blood pressure is safe in older people. We will answer:
1. What is the effect of deprescribing blood pressure lowering drugs on hospital admissions and death?
2. Does deprescribing improve quality of life and/or save money for the NHS?

Building on our previous trial of 569 people, we will aim to enrol 3,014 participants aged 75 years or older who are taking blood pressure lowering drugs, but do not have raised blood pressure readings. We will actively follow them up for one year. We will focus on those who are frail and/or with a higher risk of serious drug related side-effects. We will examine whether deprescribing is safe in this group by measuring how many people are admitted to hospital or die the year after having blood pressure lowering drugs withdrawn compared to those who continued with them. If the numbers are similar, deprescribing will be viewed as safe. If safe, we will continue the trial and passively follow-up participants using their electronic health records

for up to 10 years (subject to further funding). We will also check if deprescribing affects quality of life and/or costs for the NHS.

Who can participate?
Those aged 75 years or older and taking 2 or more blood pressure lowering drugs, but who do not have raised blood pressure readings, may be eligible to participate.

What does the study involve?
Participants will be enrolled at participating practices in England by their own GP and be required to attend a minimum of 2 appointments - a baseline assessment and one follow-up after 4 weeks. If further medications are to be stopped (for those in the intervention group) then another follow-up appointment would be required. After one year participants will be sent a questionnaire to complete remotely and the trial team will follow-up participants passively using their electronic health records for an average of 3 years (dependent on funding).

What are the possible benefits and risks of participating?
Benefits:
For those in the control group, there will be no clear additional benefits for taking part in the trial. For those in the intervention group who have their medication reduced, there is the possibility that they will be less likely to fall over, or suffer other side effects which could affect their quality of life. We will not know if this is the case until after the trial is finished.
Risks:
All participants will receive normal routine care from their GP, those in the control arm will be at no further risk by taking part. As medications which lower blood pressure also lower the risk of heart attack and stroke, those in the intervention arm may be at higher risk if their blood pressure was left unchecked. However, follow-up visits with their GP will be booked at 4 weeks following medication reduction (per medication removed) and if blood pressure is seen to rise significantly the medication will be restored rendering the likelihood of suffering an adverse event very low.
Risks are outlined in the patient information leaflet, as is a description of our data policy in order to reassure participants and provide clarity.
In order to reduce the burden of travel we have designed the study with as few visits as possible, with the majority of our outcome data being gathered remotely.

Where is the study run from?
University of Oxford (UK). This trial will be undertaken in a primary care setting, within approximately 200 general practices across all regions of the NIHR Clinical Research Network in England.

When is the study starting and how long is it expected to run for?
January 2023 to June 2026

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (UK)

Who is the main contact?
Melanie Carr, optimise2-trial@phc.ox.ac.uk
Prof Richard McManus, R.McManus@bsms.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr James Sheppard

ORCID ID
https://orcid.org/0000-0002-4461-8756

Contact details
The Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG
-
james.sheppard@phc.ox.ac.uk

Type(s)
Public

Contact name
Miss Melanie Carr

Contact details
The Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG
+44 1865 289311
optimise2-trial@phc.ox.ac.uk

Type(s)
Principal investigator

Contact name
Prof Richard McManus

ORCID ID
https://orcid.org/0000-0003-3638-028X

Contact details
Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG
-
R.McManus@bsms.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1006598

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
16667, IRAS 1006598, CPMS 56390

Study information

Scientific Title
Optimising Prescription of Treatment In older patients with Mild hypertension at Increased risk of Serious adverse Events (OPTIMISE2)

Acronym
OPTIMISE2

Study objectives
Primary objective:
To determine if deprescription of blood pressure medication in a group at higher risk of side effects results in patients attending hospital or dying during follow-up which is non-inferior (within 5%) to that observed under usual care

Secondary objectives:
To determine the difference in heart attack, stroke, heart failure, falls, fracture, dementia, high blood pressure requiring hospitalisation, other cause hospitalisation, and death in those whose medication has been withdrawn when compared to usual care. We will also look at the difference in adverse events, side effects and admissions to nursing home or care facility. Medication burden and quality of life will be assessed in both groups. Cost-effectiveness of medication withdrawal both long and short term will be assessed.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 15/09/2023, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048227; leicestercentral.rec@hra.nhs.uk), ref: 23/EM/0054

Study design
Interventional randomized parallel group controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
The trial intervention is step down anti-hypertensive medication reduction versus usual care. Randomisation will be performed using a fully validated web-based randomisation system (Sortition) with stratification factors. Those in the intervention group will initially have one medication withdrawn (as chosen by their GP) while those in the usual care arm continue with their medication as prescribed. Participants in both trial arms will attend a baseline visit and a 4-week safety follow-up visit. Those in the intervention arm may have a second medication withdrawn at this visit, if so then another visit would be required in 4 weeks, and so on for as many medications are withdrawn. All participants will be followed-up passively via health records and be asked to complete questionnaires after one year.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Antihypertensive medication reduction

Primary outcome(s)
Emergency hospitalisation (all-cause admissions which are unpredictable and at short notice because of clinical need; [admission for at least 1 day overnight]) or death measured at 1 year post-randomisation

Key secondary outcome(s))
Measured through remote assessment of health records at 1 year post-randomisation:
1. Major cardiovasular events (Four-point definition: non-fatal acute myocardial infarction, non-fatal stroke, non-fatal heart failure and cardiovascular death)
2. Myocardial infarction
3. Stroke
4. Heart Failure
5. Falls
6. Serious hypotension
7. Serious syncope
8. Serious fracture
9. Dementia
10. Serious Adverse Events

11. All-cause death, adverse events, adverse drug withdrawal events, admission to nursing home or care facility through remote assessment of health records at 1 year post-randomisation.
12. Maintenance of medication reduction through to follow-up through remote questionnaires and assessment of health records at 1 year post-randomisation.
13. Average blood pressure and perceived side effects between groups through remote

assessment of health records at 1 year post-randomisation.
14. Participants experiencing clinical events at long-term follow-up through remote assessment of health records at 3, 5, and 10 years post-randomisation (subject to further funding).
15. Participant attitudes towards deprescribing through remote questionnaire at 1 year post-randomisation
16. Initial and long-term cost-effectiveness of implementing deprescribing through remote questionnaires, assessment of health records, and extrapolation of trial outcomes encompassing 1 year post-randomisation

Completion date
30/06/2026

Eligibility

Key inclusion criteria
1. Willing and able to give informed consent for participation in the trial (or with Personal Legal Representative consent)
2. Willing and able to report any safety concerns or with a suitable carer able to report these if unable
3. Registered at either a practice using electronic health record systems (e.g. EMIS or SystmOne) or contributing to or willing to contribute to ORCHID
4. Aged 75 years or above at recruitment.
5. Controlled systolic blood pressure, defined (in accordance with NICE 2019 guidelines) as less than 140 mmHg (if aged 75-79 years) or less than 150 mmHg (if aged 80 years or above). Systolic blood pressure level will be based on screening measurements taken at baseline (mean of the 2nd and 3rd readings taken in a standardised manner) or from patient records.
6. Prescribed two or more antihypertensive medications for at least 12 months prior to trial entry. Antihypertensive medications defined as any ACE inhibitor, angiotensin II receptor blocker, calcium channel blocker, thiazide and thiazide-like diuretic (including loop diuretics), potassium-sparing diuretic, alpha-blocker, beta-blocker, vasodilator antihypertensives, centrally acting antihypertensives, direct renin inhibitors, adrenergic neurone blocking drugs.
7. Stable dose of antihypertensive medications for at least four weeks prior to trial entry.
8. Moderate or severe frailty (defined by an eFI score ≥0.20) and/or high risk (>5%) of hypotension, syncope or falls in the next 5 years, based on STRATIFY risk prediction algorithms applied to an individual’s electronic health record.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
75 years

Upper age limit
120 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Heart failure due to left ventricular systolic dysfunction (LVSD) prescribed only ACE inhibitors /angiotensin II receptor blockers and/or beta-blockers and/or spironolactone (removing any of which would be contraindicated).
2. Heart failure diagnosis without a coded echocardiogram (might have undiagnosed LVSD and a compelling need for ACEI/ angiotensin II receptor blocker and beta-blockers).
3. Suffered a myocardial infarction or stroke within the past 6 months.
4. Secondary hypertension or previous accelerated or malignant hypertension.
5. Lacking capacity to give consent and without a consultee present at the point of screening.
6. Participating in any other randomised controlled trial of drug treatment or interventional medical devices in the past 4 weeks (can be re-invited subsequently).

(added 19/12/2024)
7. Investigator deems that there is a compelling indication for medication continuation.

Date of first enrolment
10/10/2023

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
All Research Delivery Networks in England
-
-
England
-

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

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

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.
optimise2-trial@phc.ox.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	12/09/2023	11/10/2023	No	Yes
Participant information sheet	version 3.0	27/06/2025	04/12/2025	No	Yes
Protocol file	version 3.0	19/03/2024	19/12/2024	No	No
Protocol file	version 5.0	28/10/2025	04/12/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes