

Optimising Treatment for High Blood Pressure in People at Risk of Adverse Events

Participant Information Leaflet

- We would like to invite you to take part in a research trial.
- Many people take drugs to lower their blood pressure and reduce their risk of stroke and heart attacks.
- After many years of treatment, the benefits of taking these drugs **may** become outweighed by the risk of falls and other side effects (otherwise known as ‘adverse events’).
- This trial is looking to assess the safety of reducing the number of drugs prescribed to older people who have blood pressure considered to be in the normal range.
- Before you decide if you would like to take part, we would like you to understand why the research is being done and what it would involve for you.

OPTIMISE2 Trial: Overview

1. Why have I been chosen? (See page 5)

Because you are aged 75 years or older and take two or more medications to manage your blood pressure. We would like to see if reducing the number of these medications can be done safely.

2. What will I have to do? (See pages 6-9)

If you agree to take part, you will agree to be put into one of two groups, at random (equivalent to tossing a coin):

A:

A **'control'** group
where nothing about
your care will change

B:

An **'intervention'**
group where you will
have one or more
blood pressure
medication/s removed,
decided by your doctor

There is a 1 in 2 chance you will be allocated to the intervention group. During the trial, you will be asked to visit your GP surgery at least twice, for appointments with your doctor or the research team. It may be possible for the initial visit to be done remotely but any follow-up visits would need to be in person at the surgery. During these visits you will be asked to answer some questions about yourself and complete some questionnaires. We will also measure your height, weight and blood pressure. If you are in the intervention group and your blood pressure remains in the normal range after one drug has been removed, your doctor may decide it is appropriate to remove another one. This would involve another follow-up visit 4 weeks later. Your active involvement in the trial will last for 12 months. At the end of this period we will send you some questionnaires to complete.

3. What is the intervention being tested?
(See page 10)

If you are allocated to the intervention group, your doctor will choose to stop one or more of the medications you take to lower your blood pressure (only one at a time)

4. Risks and benefits of participation
(See page 11)

If you are in the control group, there are no risks or benefits to taking part relative to standard care. If you are in the intervention group, your blood pressure could rise, leading to an increased risk of heart attack or stroke. However, your GP will monitor your blood pressure carefully so the likelihood of this happening is very low. Those in the intervention group may be less likely to suffer side effects from medication such as falls.

5. Stopping participation in the trial
(See page 12)

You are free to leave the trial at any point and your decision to do so will not affect the treatment you receive from your GP. You may restart your blood pressure medication (if in the intervention group), withdraw from visits/questionnaires only, or leave the trial completely and request that we collect no more follow-up data (unless needed for safety reasons).

6. What to do if there are problems
(See page 14)

If you have any queries about this trial then please contact the trial manager on 08081968649 or email optimise2-trial@phc.ox.ac.uk

If you wish to complain about any aspect of the way in which you have been treated during the trial, you should contact the Trial Manager, or the University of Oxford's Research Governance, Ethics & Assurance (RGEA) office on 01865 572224 or email RGEA.Sponsor@admin.ox.ac.uk.

7. Confidentiality
(See pages 13-15)

All data will be kept securely according to the UK General Data Protection Regulation (GDPR) and Data Protection Act 2018. Information held and maintained by Department of Health national data centre (NHS England; <https://digital.nhs.uk>) will be used in a pseudonymised format to provide information about your health status during the follow-up period. All trial information collected will be made pseudonymous (replacing any of your directly identifiable data, such as name, with a code, such as a trial number) at the earliest practical opportunity.

8. What will happen to the results of the trial?
(See page 16)

The results of this research trial will be published in a scientific medical journal and on the study website. www.optimise2.org

9. Who funded and approved the trial?
(See page 16)

This trial is being funded by the National Institute for Health Research Health Technology Assessment. It has been reviewed and given favourable opinion by East Midlands - Leicester Central Research Ethics Committee.

Thank you for considering taking part in this trial.

OPTIMISE2 Trial: Full Details

What is the purpose of the trial?

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 three 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.

Why have I been invited to take part?

You have been invited to take part because you have, at least in the past, had high blood pressure and your doctor has given you medications to reduce it. Now that you are older, the benefits of reducing your blood pressure may be outweighed by the side effects of taking these medications (for example, with an increased risk of falling over). We would like to recruit 3,014 people like you, to see if reducing the number of blood pressure lowering medications you take can be done safely, and potentially improve your quality of life. Your GP has reviewed our trial criteria and identified you as someone who is potentially eligible.

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Do I have to take part?

No. It is up to you to decide to join the trial and if you do, you are free to withdraw at any time, without giving a reason. This would not affect the care you receive from your doctor.

What will happen to me if I take part?

If you decide you would like to take part you will be invited to a consultation with your GP. This consultation may be done remotely by telephone or using the surgery's information governance (IG) approved video conference software if face-to-face visits are not possible. They will give you some more information, explain what you would have to do and answer any questions you have. *If you would like to participate you will be asked to sign a consent form.* If you feel unsure you can ask to have another consultation and longer to think before starting the trial. If this consent visit is done remotely you will be sent an email link to complete and sign the consent form using a finger, stylus or biometric eSignature on your device.

Once you have signed the consent form, a trained researcher will ask you some basic questions about yourself (e.g. age, ethnicity, whether you smoke, etc.) and your medical history. They will also take some measurements of your height, weight and blood pressure. If this visit is remote then we may ask you to measure these yourself, or we will use the most recent record from your clinical notes. Finally, you will be asked to complete some simple questionnaires about your daily activities and general quality of life.

Following these consultations you will be randomly allocated by a computer (equivalent to tossing a coin) into one of two groups.

**What will
happen to me
if I take part?
(Continued)**

Neither you, your GP nor the research team can choose which group you will be in. This is to make sure both groups are the same to start with, so that we can accurately compare if reducing the number of medications you take is safe and beneficial.

If you are allocated to the 'control' group, you will continue with your current medication, nothing will change.

If you are allocated to the 'intervention' group, you will be asked to stop taking one or more of your blood pressure medications. This will be decided by your doctor. You will only be asked to stop one medication at a time and only if your blood pressure remains stable. Each medication removed would be followed by another visit at 4 weeks to monitor your blood pressure and check for any side effects. If you have any health concerns after having your medication stopped please contact your GP before the 4-week safety visit.

Both groups will be invited back for a follow-up visit at 4 weeks and asked to complete a questionnaire after 1 year. The questionnaire can be completed online by clicking a link in an email from our trial system or you can choose to complete it on paper and we will provide a pre-paid envelope to send it back. If you have questions or would like help completing this questionnaire then a member of the trial team can assist via phone. *There is a 1 in 2 chance you will be in the group taking fewer medications to lower blood pressure.*

Throughout this time period you will remain in the same group you are assigned to at the beginning. You will need to continue taking the treatment as

indicated unless specifically advised to stop by your GP. You can continue any other medication you normally take.

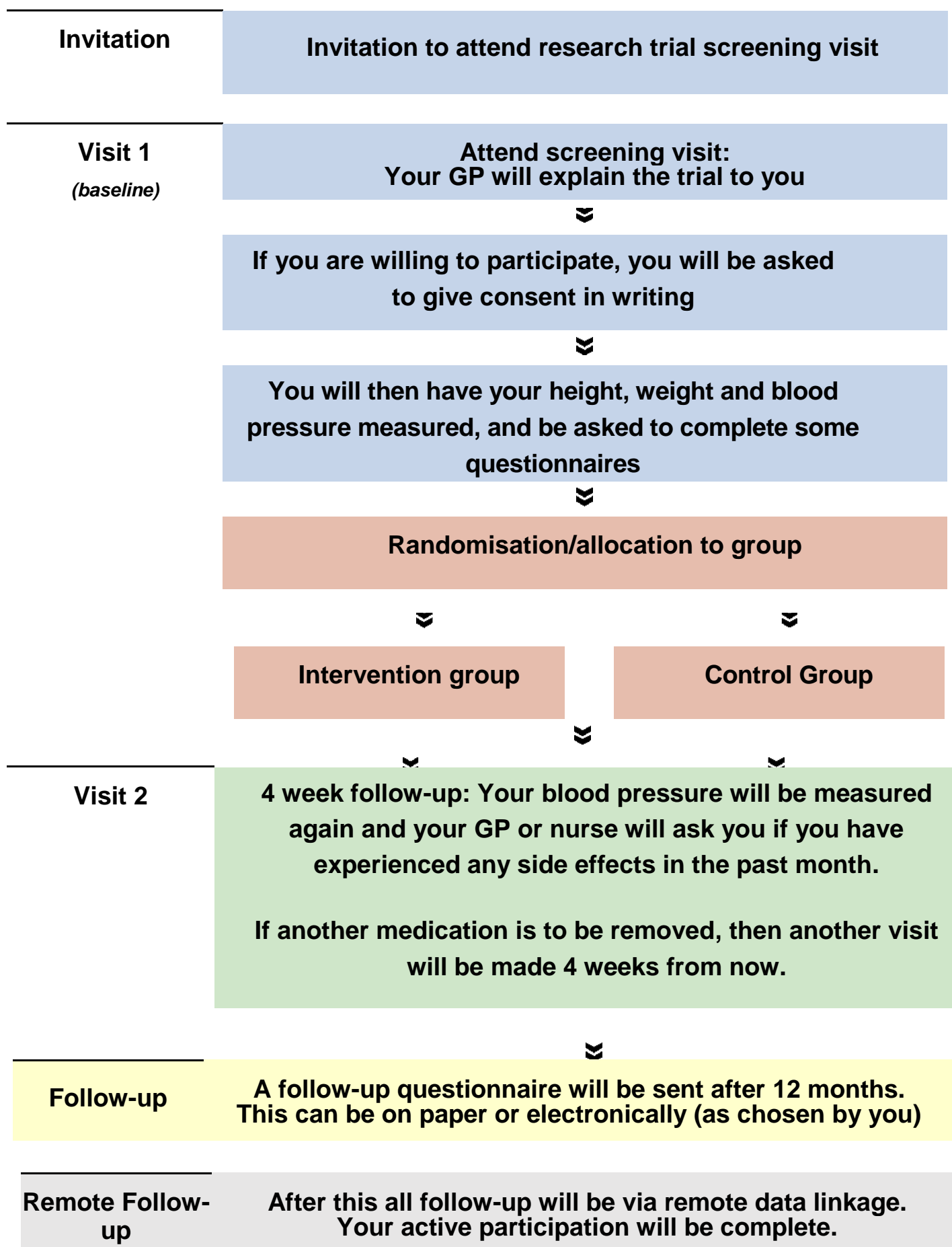
What should I consider?

There are some reasons that you may not be able to take part in the trial, including:

- Heart failure diagnosis
- If you have suffered a heart attack or stroke within the past 6 months.
- If you are participating in any other trial of drug treatment or interventional medical devices in the past 4 weeks.

All criteria will be reviewed by your GP to ensure eligibility.

Flowchart for Trial Visits



What is medication reduction?

If you are allocated to the intervention group, your doctor will choose to stop one of the medications you take to lower your blood pressure. Their decision will be based on whether you have ever experienced any side effects taking the drug, or if there is a possibility that it might react negatively with some of the other drugs you take. If neither is the case, they may choose to remove the drug you were most recently prescribed. Your GP will discuss this medication reduction plan with you at your baseline visit before you are asked to consent to the study but they will not tell you which drugs they have chosen to remove. You will be told this if allocated to the intervention group but not before. If your blood pressure remains in a normal range after the drug has been removed, your doctor may decide it is appropriate to remove another one. Every time they remove a drug, they will monitor your blood pressure carefully and invite you for a 4 week follow-up visit.

Expenses and Payment

You will not be paid for taking part in the trial. However, you will have made a valuable contribution towards research which helps to develop better ways of caring for people with high blood pressure as they get older.

What are the risks and benefits of taking part in this trial?

Risks of taking part

1. All participants in this trial will receive normal routine care from their GP. If you are in the control group, you will be at no further risk (compared to standard care) by taking part.
2. Medications which lower your blood pressure also lower your risk of having a heart attack or stroke. Thus, if you are in the intervention group and one is removed, your blood pressure may rise and if this were left unchecked, you could be at risk of suffering a heart attack or stroke (an adverse event). With the withdrawal of certain medications there may be a risk of palpitations, peripheral oedema (excess fluid causing swelling), or prostatism (swelling of the prostate gland - only relevant for people with prostates).
3. In this trial, you will see/speak to your GP at regular intervals. If blood pressure does increase significantly, your GP will reinstate your medications, *rendering the likelihood of you suffering an adverse event very low.*

Benefits of taking part

1. If you are in the control group, there will be no clear additional benefits for you taking part in the trial. However you will have the knowledge that you have contributed to research which helps to develop better ways to care for people with high blood pressure as they get older.
2. If you are in the intervention group and have your medication reduced, there is the possibility that you will be less likely to fall over or suffer other side effects which could affect your quality of life. We will not know if this is the case until after the trial is finished.

What if I become unwell during the trial?

If you become unwell, need to attend hospital for any reason or change your normal medication whilst you are in the trial you should inform your GP. We will need to record this in our trial documents. If you are in the intervention group and become unwell as a result of having your medication reduced, your GP may ask you to start taking that tablet again. You can request to start taking your medication again at any time.

What happens to me after the research visits are finished?

Your active participation in the trial will continue for 12 months. After this you will be followed up by the research team for a period of up to 10 years after you join the trial, using your medical records and data held about you in central NHS registries and databases (including NHS England). This will be used to collect information on any hospital admission or other relevant health condition that you may have during the follow up period. Your blood pressure will continue to be managed by your GP, and this may include continuing/starting medication reduction where appropriate.

What if new relevant information becomes available during the trial?

Sometimes we get new information about the treatment or strategy being studied. If this happens, your GP will tell you and discuss whether you should continue in the trial. If you decide not to carry on, your GP will make arrangements for your care to continue as per standard practice. If you decide to continue in the trial they may ask you to sign a form outlining the discussion.

What will happen if I want to stop taking part in the trial?

You are free to leave the trial at any point. Leaving the trial will not affect the treatment you receive from your GP. If you have any concerns once you have left the trial you can contact the research team for help and advice.

What will happen to my data?

All data will be kept securely according to the UK General Data Protection Regulation (GDPR) and Data Protection Act 2018 and the research team have a duty of confidentiality to you as a research participant. All data will be stored securely on a password protected database and only the research team will be able to access the information.

Information held by the Department of Health national data centre (NHS England; <https://digital.nhs.uk>) will be used in a pseudonymised format (replacing any information which could identify you with a trial identifier) to provide information about your health status during the follow-up period. We will need to send your NHS number and another identifier, likely date of birth, to NHS England so that they can provide follow-up information about any hospital admission or relevant health condition you may have. We will not be sending any information that they do not already hold and we will not share this information with anyone else. If we use telephone software for interpretation we may need to provide them with access to some of your data in order to contact you. If so, these will be approved by the University of Oxford and appropriate data access and retention policies put in place. Video calls made by GPs will be using their own pre-approved software which will have gone through Information Governance processes for clinical use. Video calls from the central trial team would use MS Teams.

Will my participation be kept confidential?

Yes, all information about you and your health will be kept private. All trial information collected will be made pseudonymous (with personal details removed) at the earliest practical opportunity. The information you provide at the first consultation and subsequent appointments will be coded with a trial identification number, so you cannot be identified from it by anyone other than the research team. Research data

**Will my
participation
be kept
confidential?
continued**

generated by the study will be held for 20 years but we will not keep identifiable information about you after the trial has finished long-term follow-up and data cleaning, except to contact you to inform you of the publication of results. This excludes any research documents with personal information, such as consent forms, which will be held securely at the University of Oxford for at least 12 months-3 years after the end of the trial. Responsible members of the University of Oxford, or the regulatory authorities (MHRA) may be given access to your medical and research records for monitoring and/or audit of the trial to ensure the research is complying with applicable regulations.

The University of Nottingham's PRIMIS team will extract follow-up data about you from GP Practice systems on our behalf. PRIMIS have an agreement in place with the University of Oxford and your GP practice for this data extraction. PRIMIS will not review or store the data, only extract it from the GP system and securely transfer it to the trial team.

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' Data protection regulation provides you with control over your personal data and how it is used. However, when you agree to your information being used in research, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at:

<https://compliance.web.ox.ac.uk/individual-rights>

The trial information may be provided to researchers running other research trials within the University of Oxford, other Universities, the NHS, or abroad if requested.

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Will my participation be kept confidential? continued

Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

If you choose to withdraw from active participation in the trial we would still like to collect relevant information about your health, as this will be invaluable to our research. If you would also like to withdraw consent for the collection of further data you can still do so.

The local study team (based at your GP practice) will use your name, NHS number, home address, and contact details, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. The consent form you complete for this study will be kept for at least 12 months - 3 years after the study has finished.

What if there are any problems?

If you have any queries about this trial then please contact the Trial Manager (see contact details on page 17).

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this trial, you should contact the Trial Team (see page 16), or you may contact the University of Oxford Research Governance, Ethics & Assurance Team (RGEA) office on 01865 572224 or email: RGEA.Sponsor@admin.ox.ac.uk

The NHS Patient Advice and Liaison Service (PALS) is available at <http://www.pals.nhs.uk/> PALS is a confidential NHS service that can provide you with support for any complaints or queries you

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**What if there are any problems?
continued**

may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment with which you are provided.

What will happen to the results of the research trial?

The results of this research trial will be published on the trial website (www.optimise2.org) and in a scientific journal, sometime after the trial has finished. Your individual results will not be identifiable nor would you be identified in any report or publication. Your GP will have access to your personal results, which will be stored in your medical notes, and will address any that are unusual.

Who is organising and funding the research?

This trial is being funded by the National Institute for Health Research (NIHR) Health Technology Assessment. The trial is being run by Primary Care Clinical Trials Unit, Nuffield Department of Primary Care Health Sciences, University of Oxford.

Who has reviewed the trial?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by East Midlands - Leicester Central Research Ethics Committee. Members of the OPTIMISE2 Patient & Public Involvement Group have reviewed this leaflet and contributed feedback.

This trial has also received approval from the Medicines and Healthcare products Regulatory Agency (MHRA).

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**Further
information and
contact details**

If you would like any further information about this trial you can call the research team on 08081968649 or e-mail at optimise2-trial@phc.ox.ac.uk

Our Contact Details

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