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Screening for atrial fibrillation with ECG to reduce stroke – a randomised controlled trial

Submission date	**Recruitment status**	[X] Prospectively registered
02/03/2020	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
11/03/2020	Ongoing	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
02/05/2024	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 22/02/2022:

Background and study aims
Atrial fibrillation (AF) is a heart condition that causes an irregular heartbeat. It affects up to 1 in 10 people over the age of 65. AF greatly increases the risk of stroke, but treatment with blood-thinning (anticoagulant) medication can stop this happening. About 10% of strokes happen in people unaware they have AF. Detecting AF can be difficult because it often comes and goes, and may not cause symptoms. Many clinicians think the NHS should promote AF screening. The UK National Screening Committee has highlighted a lack of evidence that detecting AF in people by screening would benefit them. Researchers are therefore undertaking a large 8-year programme of work to find out if screening for AF in people aged 70 and over does prevent stroke and other problems like heart attacks, does not cause significant harm, and represents good value for money for the NHS. This study will address these questions.

Who can participate?
People aged 70 or over

What does the study involve?
Internal Pilot Trial: Participating practices will be randomly allocated to the intervention (AF screening) group or the control group.
Main Trial: Participants will be randomly allocated to the intervention (AF screening) group or control group.
Consented participants in the intervention group will be invited to take part in AF screening (see below for more details). The control group do not receive any interventions. Data collection will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 4-year follow-up. Consented participants in the intervention group will be invited to take part in screening for atrial fibrillation. The screening consists of 3 weeks of intermittent ECG screening at home. The screening process will be administered remotely by post/phone. The single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) will be posted to the patient with instructions for how to use it. Support will be provided by phone. The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. Each ECG records

for 30 seconds. The researchers will request ECG traces are recorded four times per day (plus when symptomatic) for 3 weeks. Participants will be asked to return the ECG recorder by post at the end of the screening period. ECGs will be reviewed once the ECG recorder is returned. ECGs tagged as 'possible AF' will be reviewed by a trained individual for cases of AF or other important rhythm disturbances. The researchers will send diagnostic results to the practice. The practice will inform all participants of their screening result following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice by 12 weeks from the date they return the ECG recorder. This timescale is in line with current NHS screening programmes. Participants with confirmed AF will be invited for a consultation with the GP (or other healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy. Other rhythm abnormalities, in addition to AF, may also be detected although these are not being actively sought. Such ECGs will be reviewed by a trained individual and reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. This completes the participant involvement in the screening process. Baseline and follow-up (approx. annually) data from the GP medical record will be collected in accordance with the consent provided.
Internal Pilot Trial: A random sample of patients will be assessed by postal questionnaire on up to three occasions. Participants from various stages of the study will be invited by the trial team to take part in interviews conducted by telephone. Interviews will be audio recorded.

What are the possible benefits and risks of participating?
Taking part in the study may bring participants a sense of altruism in that it will be the world's largest randomised trial for AF screening. Knowing that the programme aims to prevent strokes and heart attacks in people just like them in the future may have a positive mental effect on the participant. Patients diagnosed with AF will be offered treatment which will greatly reduce their risk of having a stroke or heart attack, and possibly dementia. It is possible that a non-AF clinically significant cardiac rhythm abnormality may be diagnosed, in which case the patient will be referred to their GP for appropriate care - this may include further tests and/or treatment if necessary.

Where is the study run from?
1. NIHR CRN: Eastern
2. NIHR CRN: North East and North Cumbria
3. NIHR CRN: North West Coast
4. NIHR CRN: Yorkshire and Humber
5. NIHR CRN: Greater Manchester
6. NIHR CRN: East Midlands
7. NIHR CRN: West Midlands
8. NIHR CRN: West of England
9. NIHR CRN: Thames Valley and South Midlands
10. NIHR CRN: Kent, Surrey and Sussex
11. NIHR CRN: Wessex
12. NIHR CRN: South West Peninsula
13. NIHR CRN: North Thames
14. NIHR CRN: South London
15. NIHR CRN: North West London

When is the study starting and how long is it expected to run for?
August 2017 to September 2028

Who is funding the study?
NIHR Programme Grant for Applied Research (UK)

Who is the main contact?
Mr Andrew Dymond
SAFER@medschl.cam.ac.uk

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Previous plain English summary as of 15/02/2021:

Background and study aims
Atrial fibrillation (AF) is a heart condition that causes an irregular heartbeat. It affects up to 1 in 10 people over the age of 65. AF greatly increases the risk of stroke, but treatment with blood-thinning (anticoagulant) medication can stop this happening. About 10% of strokes happen in people unaware they have AF. Detecting AF can be difficult because it often comes and goes, and may not cause symptoms. Many clinicians think the NHS should promote AF screening. The UK National Screening Committee has highlighted a lack of evidence that detecting AF in people by screening would benefit them. Researchers are therefore undertaking a large 8-year programme of work to find out if screening for AF in people aged 70 and over does prevent stroke and other problems like heart attacks, does not cause significant harm, and represents good value-for-money for the NHS. This study will address these questions.

Who can participate?
People aged 70 or over

What does the study involve?
Participating practices will be randomly allocated to the intervention (AF screening) group or the control group. Consented participants in the intervention practices will be invited to take part in AF screening (see below for more details). The control group do not receive any interventions. Data collection will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 5-year follow-up. Consented participants in intervention practices will be invited to take part in screening for atrial fibrillation. The screening consists of 3 weeks of intermittent ECG screening at home. The screening process will be administered remotely by post/phone to ensure participant safety during the COVID-19 pandemic. The single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) will be posted to the patient with instructions for how to use it. Support will be provided by phone. When it is safe to do so, participants requiring additional support with using the ECG recorder may be seen at their GP practice by a member of practice staff. The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. Each ECG records for 30 seconds. The researchers will request ECG traces are recorded four times per day (plus when symptomatic) for 3 weeks. Participants will be asked to return the ECG recorder by post at the end of the screening period. ECGs will be reviewed once the ECG recorder is returned. ECGs tagged as ‘possible AF’ will be reviewed by a trained individual for cases of AF or other important rhythm disturbances. The researchers will send diagnostic results to the practice. The practice will inform all participants of their screening result following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice by 12 weeks from the date they return the ECG recorder. This timescale is in line with current NHS screening programmes. Participants with confirmed AF will be invited to attend a consultation with the GP (or other healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy. Other rhythm

abnormalities, in addition to AF, may also be detected. Such ECGs will be reviewed by a trained individual and reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. This completes the participant involvement in the screening process. Baseline and follow-up (approx. annually) data from the GP medical record will be collected in accordance with the consent provided. A random sample of patients will be assessed by postal questionnaire on up to three occasions. Participants from various stages of the study will be invited by the trial team to take part in interviews, either by telephone or face-to-face. Interviews will be audio recorded.

What are the possible benefits and risks of participating?
Taking part in the study may bring participants a sense of altruism in that it will be the world's largest randomised trial for AF screening. Knowing that the programme aims to prevent strokes and heart attacks in people just like them in the future may have a positive mental effect on the participant. Patients diagnosed with AF will be offered treatment which will greatly reduce their risk of having a stroke or heart attack, and possibly dementia. It is possible that a non-AF clinically significant cardiac rhythm abnormality may be diagnosed, in which case the patient will be referred to their GP for appropriate care - this may include further tests and/or treatment if necessary.

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When is the study starting and how long is it expected to run for?
August 2017 to March 2027

Who is funding the study?
NIHR Programme Grant for Applied Research (UK)

Who is the main contact?
Mr Andrew Dymond
SAFER@medschl.cam.ac.uk

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Previous plain English summary:

Background and study aims
Atrial fibrillation (AF) is a heart condition that causes an irregular heartbeat. It affects up to 1 in

10 people over the age of 65. AF greatly increases the risk of stroke, but treatment with blood-thinning (anticoagulant) medication can stop this happening. About 10% of strokes happen in people unaware they have AF. Detecting AF can be difficult because it often comes and goes, and may not cause symptoms. Many clinicians think the NHS should promote AF screening. The UK National Screening Committee has highlighted a lack of evidence that detecting AF in people by screening would benefit them. Researchers are therefore undertaking a large 8-year programme of work to find out if screening for AF in people aged 70 and over does prevent stroke and other problems like heart attacks, does not cause significant harm, and represents good value-for-money for the NHS. This study will address these questions.

Who can participate?
People aged 70 or over

What does the study involve?
Participating practices will be randomly allocated to the intervention (AF screening) group or the control group. Consented participants in the intervention practices will be invited to attend an AF screening visit (see below for more details). The control group do not receive any interventions. Data collection will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 5-year follow-up. Consented participants in intervention practices will be invited to take part in screening for atrial fibrillation. The screening will be carried out in two stages: an initial screen at the practice, followed by 3 weeks of intermittent screening at home. A member of staff will assign a single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) to the patient and instruct them how to use it. Each ECG records for 30 seconds. The participant will be sent home with the ECG recorder and instructions for use. The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. The researchers will request ECG traces are recorded four times per day (plus when symptomatic) for 3 weeks. Participants will be asked to return the ECG recorder to the practice at the end of the screening period. ECGs will be reviewed once the ECG recorder is returned. ECGs tagged as ‘possible AF’ or ‘other deviations’ will be reviewed by a trained individual for cases of AF or other important rhythm disturbances. The researchers will send diagnostic results to the practice. The practice will inform all participants of their screening result following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice by 12 weeks from the date they return the ECG recorder to the practice. This timescale is in line with current NHS screening programmes. Participants with confirmed AF will be invited to attend an appointment with the GP (or other healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy. Other rhythm abnormalities, in addition to AF, may also be detected. Such ECGs will be reviewed by a trained individual and reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. This completes the participant involvement in the screening process. Baseline and follow-up (approx. annually) data from the GP medical record will be collected in accordance with the consent provided. A random sample of patients will be assessed by postal questionnaire on up to three occasions. Participants from various stages of the study will be invited by the trial team to take part in interviews, either by telephone or face-to-face. Interviews will be audio recorded.

What are the possible benefits and risks of participating?
Taking part in the study may bring participants a sense of altruism in that it will be the world's largest randomised trial for AF screening. Knowing that the programme aims to prevent strokes and heart attacks in people just like them in the future may have a positive mental effect on the participant. Patients diagnosed with AF will be offered treatment which will greatly reduce their

risk of having a stroke or heart attack, and possibly dementia. It is possible that a non-AF clinically significant cardiac rhythm abnormality may be diagnosed, in which case the patient will be referred to their GP for appropriate care - this may include further tests and/or treatment if necessary.

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When is the study starting and how long is it expected to run for?
August 2017 to March 2026

Who is funding the study?
NIHR Programme Grant for Applied Research (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
272184

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 43549, IRAS 272184

Study information

Scientific Title
The SAFER Trial: Screening for Atrial Fibrillation with ECG to Reduce stroke - a randomised controlled trial

Acronym
SAFER

Study objectives
This trial aims to find out if screening for atrial fibrillation (AF) in people aged 70 and over does prevent stroke and other problems like heart attacks and represents good value-for-money for the NHS.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/10/2019, London Central NRES (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8012; NRESCommittee.London-Central@nhs.net), REC ref: 19/LO/1597

Study design
Randomized; Both; Design type: Screening, Other, Qualitative

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Atrial fibrillation

Interventions

Current interventions as of 22/02/2022:

This trial has been carefully designed in consultation with the UK National Screening Committee to mimic as closely as possible a 'real life' national screening programme. There is no point in testing an artificial 'research' version of a screening programme, as if this was found to be feasible and rolled out by the NHS it would most likely fail.
Internal Pilot Trial: The researchers will recruit 39 practices, who will each invite around ~1,200 eligible patients to take part in the trial. Participants will provide written consent by post. Following this, practices will be randomised to intervention (AF screening) or control in the ratio 1:2. Consented participants in the intervention practices will be invited to take part in AF screening (see below for more details). The control group do not receive any interventions.
Main Trial: The researchers will recruit ~ 170 practices in order to recruit ~82,000 patients. Participants will provide written consent by post. Following this, participants will be randomised to either intervention (AF screening) or control in a ratio 1:2. Consented participants in the intervention group will be invited to take part in AF screening (see below for more details). The control group will not receive any interventions.
Data collection for the whole trial will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 4-year follow-up.

Some participants will also be invited to complete questionnaires and to take part in qualitative work including interviews and observations. There is an extensive health economic modelling work package in the trial, as a critical factor in determining the success of the screening programme will be value for money for the NHS. There are 3 types of participants in this trial; patients (the largest group), practice and trial staff, and additional healthcare professionals /external stakeholders. The latter two groups will be invited to participate in qualitative components only. Each of these participant types will be considered in turn:

1. Patients
Practices will identify potentially eligible patients >= 70 years with an electronic record search and invite about ~1,200 to take part in the trial in the Internal Pilot Trial, and invite all eligible patients in the Main Trial. The researchers may also use this opportunity to over-sample specific substrata e.g. the very elderly, if they observe at early stages that they are under-represented. The practice will send identified patients an invitation pack consisting of a participant information sheet (PIS), covering letter, consent form, a negative reply slip (not all practices) and Freepost envelope. The PIS and consent form will focus on participation in the wider trial and the request to access and follow up the patient’s electronic health records. It will explain that this is for a trial of stroke prevention, and that participants may be contacted to participate in screening, and can decide at that point whether to accept or decline the screening invitation. The negative reply slip will enable patients who do not wish to consent to respond anonymously indicating their reasons for declining the trial invitation. It will also provide an option for patients who do not wish to participate to indicate that they would be happy for a researcher to contact them to discuss further their reasons for deciding to not participate. This is a key part in understanding whether there is anything about the concept of screening that is putting patients off consenting. If the patient wishes to take part in the trial they will be invited to complete the consent form and return it to the trial team in the Freepost envelope provided or to complete an online consent form (this process will be managed by the trial team).

Following participant consent, the practice (Internal Pilot Trial) or participants (Main Trial) will be randomised to intervention (AF screening) or control at a ratio of 1:2. Consented participants in the intervention group will be invited to take part in screening for atrial fibrillation. They will be sent an additional PIS about the screening process and its potential benefits and harms – consistent with a national screening programme leaflet. This invitation needs to be separate

from the main research trial invitation as the researchers need to be able to specifically test a screening invitation leaflet of the type (in terms of content, language and tone) that would be used in an NHS national screening programme. Conflating the two information leaflets would make this impossible.

The researchers may also use SMS messages from the practice as part of the recruitment process. This method of communication is increasingly commonly used by practices for communication about routine care in patients in this age group with a great deal of success. It is likely that it would be utilised in national roll-out of an AF screening programme. Some practices may wish to also invite patients to a trial-specific meeting, as part of the invitation to the screening process. Here AF screening is presented and patients are able to ask questions. This approach is used in research practices in the local region to good effect.

Some participants will also be invited at various points in the screening process to take part in additional, optional qualitative interviews. The initial trial invitation PIS will introduce these elements stating that additional information will be provided at the point of invitation to these elements, and the participant is free to decide at that point whether to take part or not. A decision not to take part will not affect their participation in the main trial. The researchers will carefully sample participants for an invitation to take part in these elements to ensure that they are not overburdened by invitations to participate in multiple qualitative aspects. Please see the qualitative section towards the end of this question for more details of these components.

The screening consists of 3 weeks of intermittent ECG recording at home.

A single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) will be sent by post to the participant with full instructions for how to use it. Support will be provided by phone.

The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. In the STROKESTOP trial, sufficient adherence (at least 15 ECG traces) was achieved by 99% of participants (aged 75). Observations from the SAFER feasibility study suggest excellent adherence to 4 ECGs per day across age groups.

The researchers will request ECG traces are recorded four times per day (plus when symptomatic) for 3 weeks. In order to maximise adherence to ECG recording they may intervene by contacting the participant if the Zenicor system alerts that no ECGs have been received from a device for a certain number of days, or if a significant proportion of unclear traces are recorded.

Prior to participants starting screening the researchers will send an email, where possible, including the link to the patient ECG recording instruction video on the trial website. This is to try and ensure clear traces are recorded in order to facilitate review and diagnosis by the cardiologists.

Participants will be asked to return the ECG recorder by post at the end of the screening period.

ECG reading system:
The ECG traces are not displayed on the recorder, but are transmitted via mobile signal to a central secure Zenicor database from where they are viewed via a web-based platform. At the end of the screening period when the ECG recorder is returned the patient will be flagged on the system as complete and ready for review. The system algorithm classifies and tags each ECG trace as ‘no tag’, ‘possible AF’’ or ‘poor quality’. ECGs tagged as ‘possible AF’ will be reviewed by

a suitably qualified individual. A trial cardiologist will diagnose AF or any other important rhythm disturbance. The researchers will not require a 12-lead ECG to be undertaken, as single lead ECGs read by cardiologists have high accuracy. Review and subsequent classification of ECGs, including diagnosis and additional information for the GP occurs within the web-based platform.

Screening results:
The trial team will send patient screening results to the practice. The practice will record the information on the patient medical notes. In addition, a full report including cardiologist diagnosis, comments and a copy of relevant ECG traces will be sent to the practice for each patient with a positive (AF or other) diagnosis. The GP will also be provided with access to the Zenicor online system to view and download the ECG traces and reports for all their patients taking part, should they wish to do so. An expedited results pathway will be available for any screening results the cardiologist identifies as clinically urgent. All participants will be notified of their screening result by the practice, following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice within 12 weeks from the date they return the ECG recorder. This timescale is in line with current NHS screening programmes.

Management of participants with AF:
Participants with confirmed AF will be invited to have a consultation with the GP (or other appropriate healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy.

Incidental cardiac findings:
The algorithm that interrogates each ECG trace is set to optimise identification of AF, and is not set to pick up non-AF findings. However, if another significant arrhythmia is detected this will reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. The report will recommend to the GP if any further action is necessary, including possible referral. The PIS makes it clear to participants that other (non-AF) rhythm abnormalities may be detected as a result of screening.

This completes the participant involvement in the screening process. Baseline and follow-up data from the GP medical record will be collected in accordance with the consent provided.

Questionnaires – a random sample of patients from the Internal Pilot Trial (2,376; 1,512 invited to screening and 864 not invited to screening, matched for age and sex where possible) will be assessed by postal questionnaire at baseline (pre-invitation) and post-invitation (8 weeks and ~6 months). Participants will be sent the questionnaire (consisting of 3 validated measures to assess psychological and functional status) with a covering letter and freepost envelope. An online completion option will be provided. Consent will be assumed by completion and return.

Qualitative components:
In addition to the screening process outlined above a small number of patients will also be invited to participate in one or more qualitative components of the trial. The qualitative components of this programme of work will explore how screening is implemented at a practice level, and examine in some detail how practice and trial staff and patients experience the AF screening intervention. Understanding the necessary and sufficient conditions for increased detection of AF and increased use of anticoagulation for screen-detected cases is essential in developing a feasible and sustainable screening programme, both within the main trial and nationally. These activities will be conducted in a small sub-sample of screening practices.

Interviews – participants from various stages of the trial will be invited by the trial team to take part in interviews, either by telephone or face-to-face (when considered COVID-safe). These may be one-off interviews (patients who decline the offer of taking part in the trial but agree to speak to a researcher about their reasons, and participants who decline the offer of screening), longitudinal interviews (following individual participants through the screening process with up to 4 interviews, the initial interview face-to-face with subsequent interviews conducted by telephone) or interviews about the meaning and implications of an AF diagnosis, and the potential impact of anticoagulation on daily medication regimens. Interviews will be audio recorded.

Observations – when it is safe to do so the researchers will conduct ethnographic observations of relevant practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. These will result in the observation of patients.

2. Practice and trial staff
Interviews – the trial team will identify staff involved in the trial at the practice and approach them directly with an invitation to take part in an interview. Interviews will be conducted with GPs, nurses, practice managers, receptionists, other administrative staff, involved in the delivery of the screening programme to explore reactions to and attitudes towards the various components of the trial AF screening process. Interviews may be repeated as the delivery of the AF screening programme progresses. Trial staff will also be interviewed as they will be delivering the screening intervention centrally and remotely.

Ethnographic observations - when it is safe to do so the researchers will conduct ethnographic observations of relevant practice meetings and other practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. No photos or videos will be taken. Field notes will not include any identifiable information.

3. External stakeholders
Part of the practice case studies interview work may involve identifying relevant external stakeholders to the practice and inviting them to take part in an interview. These individuals may include local care commissioners, clinical pharmacists, training providers, for example. Interviews may be repeated as the delivery of the AF screening programme progresses.

Previous interventions as of 15/02/2021:

This trial has been carefully designed in consultation with the UK National Screening Committee to mimic as closely as possible a 'real life' national screening programme. There is no point in testing an artificial 'research' version of a screening programme, as if this was found to be feasible and rolled out by the NHS it would most likely fail. The researchers will recruit 360 practices, who will each invite around 1,000 eligible patients to take part in the trial. Participants will provide written consent by post. Following this, practices will be randomised to intervention (AF screening) or control in the ratio 1:2. Consented participants in the intervention practices will be invited to take part in AF screening (see below for more details). The control group do not receive any interventions. Data collection for the trial will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 5-year follow-up.

Some participants will also be invited to complete questionnaires and to take part in qualitative work including interviews and observations. There is an extensive health economic modelling work package in the trial, as a critical factor in determining the success of the screening programme will be value for money for the NHS. There is an internal pilot phase of 36 practices (12 screening, 24 control). There are 3 types of participants in this trial; patients (the largest group), practice and trial staff, and additional healthcare professionals/external stakeholders. The latter two groups will be invited to participate in qualitative components only. Each of these participant types will be considered in turn:

1. Patients
The researchers will recruit 360 GP practices in the UK. Practices will identify potentially eligible patients >= 70 years with an electronic record search and invite about 1,000 to take part in the trial. The researchers may also use this opportunity to over-sample specific substrata e.g. the very elderly, if they observe at early stages that they are under-represented. The practice will send identified patients an invitation pack consisting of a participant information sheet (PIS), covering letter, consent form, reply slip and Freepost envelope. The PIS and consent form will focus on participation in the wider trial and the request to access and follow up the patient's electronic health records. It will explain that this is for a trial of stroke prevention, and that participants may be contacted to participate in screening, and can decide at that point whether to accept or decline the screening invitation. The reply slip will enable patients who do not wish to consent to respond anonymously indicating their reasons for declining the trial invitation. It will also provide an option for patients who do not wish to participate to indicate that they would be happy for a researcher to contact them to discuss further their reasons for deciding to not participate. This is a key part in understanding whether there is anything about the concept of screening that is putting patients off consenting. If the patient wishes to take part in the trial they will be invited to complete the consent form and return it to the trial team in the Freepost envelope provided or to complete an online consent form (this process will be managed by the trial team).

Following participant consent, the practice will be randomised to intervention (AF screening) or control at a ratio of 1:2. Consented participants in intervention practices will be invited to take part in screening for atrial fibrillation. They will be sent an additional PIS about the screening process and its potential benefits and harms – consistent with a national screening programme leaflet. This invitation needs to be separate from the main research trial invitation as the researchers need to be able to specifically test a screening invitation leaflet of the type (in terms of content, language and tone) that would be used in an NHS national screening programme. Conflating the two information leaflets would make this impossible.

The researchers may also use SMS messages from the practice as part of the recruitment process. This method of communication is increasingly commonly used by practices for communication about routine care in patients in this age group with a great deal of success. It is likely that it would be utilised in national roll-out of an AF screening programme. Some practices may wish to also invite patients to a trial-specific meeting, as part of the invitation to the screening process. Here AF screening is presented and patients are able to ask questions. This approach is used in research practices in the local region to good effect.

During the trial in addition to screening invitation letters, the researchers will also encourage practices to opportunistically approach consented patients, for example at routine appointments, health checks, flu vaccinations, etc. Again, reminder letters and/or emails/SMS will be used if necessary. Procedures at individual practices will be adapted to fit existing practice systems as much as possible, to minimise burden and replicate the delivery of a national

screening programme. As a critical factor to the success of the trial, response rates will be closely monitored throughout and approaches and processes changed as required to optimise uptake.

Some participants will also be invited at various points in the screening process to take part in additional, optional qualitative interviews. The initial trial invitation PIS will introduce these elements stating that additional information will be provided at the point of invitation to these elements, and the participant is free to decide at that point whether to take part or not. A decision not to take part will not affect their participation in the main trial. The researchers will carefully sample participants for an invitation to take part in these elements to ensure that they are not overburdened by invitations to participate in multiple qualitative aspects. Please see the qualitative section towards the end of this question for more details of these components.

The screening consists of 3 weeks of intermittent ECG recording at home.

A single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) will be sent by post to the patient with full instructions for how to use it. Support will be provided by phone. When is safe to do so, participants requiring additional support with using the ECG recorder may be seen at their GP practice by a member of practice staff.

The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. In the STROKESTOP trial, sufficient adherence (at least 15 ECG traces) was achieved by 99% of participants (aged 75). Observations from the SAFER feasibility study suggest excellent adherence to 4 ECGs per day across age groups.

The researchers will request ECG traces are recorded four times per day (plus when symptomatic) for 3 weeks. In order to maximise adherence to ECG recording they may intervene by contacting the participant if fewer than the expected number of ECG traces are received (e.g. less than 50%), if the Zenicor system alerts that no ECGs have been received from a device for a certain number of days, or if a significant proportion of unclear traces are recorded.

When participants start their screening period the researchers will send an email (submitted for review), where possible, reiterating good ECG recording technique including the link to the patient ECG recording instruction video on the trial website. This is to try and ensure clear traces are recorded in order to facilitate review and diagnosis by the cardiologists.

Participants will be asked to return the ECG recorder by post at the end of the screening period.

ECG reading system:
The ECG traces are not displayed on the recorder, but are transmitted via mobile signal to a central secure Zenicor database from where they are viewed via a web-based platform. At the end of the screening period when the ECG recorder is returned the patient will be flagged on the system as complete and ready for review. The system algorithm classifies and tags each ECG trace as ‘no tag’, ‘possible AF’’ or ‘poor quality’. ECGs tagged as ‘possible AF’ will be reviewed by a suitably qualified individual . A trial cardiologist will diagnose AF or any other important rhythm disturbance. The researchers will not require a 12-lead ECG to be undertaken, as single lead ECGs read by cardiologists have high accuracy. Review and subsequent classification of ECGs, including diagnosis and additional information for the GP occurs within the web-based platform.

Screening results:
The trial team send patient screening results to the practice. The practice will record the information on the patient medical notes. In addition, a full report including cardiologist diagnosis, comments and a copy of relevant ECG traces will be sent to the practice for each patient with a positive (AF or other) diagnosis. The GP will also be provided with access to the Zenicor online system to view and download the ECG traces and reports for all their patients taking part, should they wish to do so. An expedited results pathway will be available for any screening results the cardiologist identifies as clinically urgent. All participants will be notified of their screening result by the practice, following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice within 12 weeks from the date they return the ECG recorder. This timescale is in line with current NHS screening programmes.

Management of participants with AF:
Participants with confirmed AF will be invited to attend a consultation with the GP (or other healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy.

Incidental cardiac findings:
The algorithm that interrogates each ECG trace is set to optimise identification of AF, and is not set to pick up non-AF findings. However if another significant arrhythmia is detected this will reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. The report will recommend to the GP if any further action is necessary, including possible referral. The PIS makes it clear to participants that other (non-AF) rhythm abnormalities may be detected as a result of screening.

This completes the participant involvement in the screening process. Baseline and follow-up data from the GP medical record will be collected in accordance with the consent provided.

Questionnaires – a random sample of patients (1,800; 1,500 invited to screening and 300 not invited to screening, matched for age, sex and postcode deprivation score where possible) will be assessed by postal questionnaire at baseline (pre-invitation) and post-invitation (8 weeks and 6 months). Participants will be sent the questionnaire (consisting of 3 validated measures to assess psychological and functional status) with a covering letter and freepost envelope. An online completion option will be provided. Consent will be assumed by completion and return.

Qualitative components:
In addition to the screening process outlined above a small number of patients will also be invited to participate in one or more qualitative components of the trial. The qualitative components of this programme of work will explore how screening is implemented at a practice level, and examine in some detail how practice and trial staff and patients experience the AF screening intervention. Understanding the necessary and sufficient conditions for increased detection of AF and increased use of anticoagulation for screen-detected cases is essential in developing a feasible and sustainable screening programme, both within the main trial and nationally. These activities will be conducted in a small sub-sample of screening practices.

Interviews – participants from various stages of the trial will be invited by the trial team to take part in interviews, either by telephone or face-to-face (when considered COVID-safe). These may be one-off interviews (patients who decline the offer of taking part in the trial but agree to speak to a researcher about their reasons, and participants who decline the offer of screening), longitudinal interviews (following individual participants through the screening process with up to 4 interviews, the initial interview face-to-face with subsequent interviews conducted by

telephone) or graphic elicitation interviews (interviewees will be supported by the interviewer to complete relational and/or sequential diagrams outlining their medical history, the meaning and implications of an AF diagnosis within this history, and the potential impact of anticoagulation on their daily medication regimens). Interviews will be audio recorded.

Observations – when it is safe to do so the researchers will conduct ethnographic observations of relevant practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. These will result in the observation of patients.

2. Practice and trial staff
Interviews – the trial team will identify staff involved in the trial at the practice and approach them directly with an invitation to take part in an interview. Interviews will be conducted with GPs, nurses, practice managers, receptionists, other administrative staff, involved in the delivery of the screening programme to explore reactions to and attitudes towards the various components of the trial AF screening process. Interviews may be repeated as the delivery of the AF screening programme progresses. Trial staff will also be interviewed as they will be delivering the screening intervention centrally and remotely.

Ethnographic observations - when it is safe to do so the researchers will conduct ethnographic observations of relevant practice meetings and other practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. No photos or videos will be taken. Field notes will not include any identifiable information.

3. External stakeholders
Part of the practice case studies interview work may involve identifying relevant external stakeholders to the practice and inviting them to take part in an interview. These individuals may include local care commissioners, clinical pharmacists, training providers, for example. Interviews may be repeated as the delivery of the AF screening programme progresses.

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Previous interventions:

This trial has been carefully designed in consultation with the UK National Screening Committee to mimic as closely as possible a 'real life' national screening programme. There is no point in testing an artificial 'research' version of a screening programme, as if this was found to be feasible and rolled out by the NHS it would most likely fail. The researchers will recruit 360 practices, who will each invite around 1,000 eligible patients to take part in the trial. Participants will provide written consent by post. Following this, practices will be randomised to intervention (AF screening) or control in the ratio 1:2. Consented participants in the intervention practices will be invited to attend an AF screening visit (see below for more details). The control group do not receive any interventions. Data collection for the trial will be electronic through GP medical notes and NHS Digital and health registry linkage, with an average of 5-year follow-up.

Some participants will also be invited to complete questionnaires and to take part in qualitative work including interviews and observations. There is an extensive health economic modelling work package in the trial, as a critical factor in determining the success of the screening programme will be value for money for the NHS. There is an internal pilot phase of 36 practices

(12 screening, 24 control). There are 3 types of participants in this trial; patients (the largest group), practice staff, and additional healthcare professionals/external stakeholders. The latter two groups will be invited to participate in qualitative components only. Each of these participant types will be considered in turn:

1. Patients
The researchers will recruit 360 GP practices in the UK. Practices will identify potentially eligible patients >= 65 years with an electronic record search and invite about 1,000 to take part in the trial. The researchers may also use this opportunity to over-sample specific substrata e.g. the very elderly, if they observe at early stages that they are under-represented. The practice will send identified patients an invitation pack consisting of a participant information sheet (PIS), covering letter, consent form, reply slip and Freepost envelope. The PIS and consent form will focus on participation in the wider trial and the request to access and follow up the patient's electronic health records. It will explain that this is for a trial of stroke prevention, and that participants may be contacted to participate in screening, and can decide at that point whether to accept or decline the screening invitation. The reply slip will enable patients who do not wish to consent to respond anonymously indicating their reasons for declining the trial invitation. It will also provide an option for patients who do not wish to participate to indicate that they would be happy for a researcher to contact them to discuss further their reasons for deciding to not participate. This is a key part in understanding whether there is anything about the concept of screening that is putting patients off consenting. If the patient wishes to take part in the trial they will be invited to complete the consent form and return it to the trial team in the Freepost envelope provided or to complete an online consent form (this process will be managed by the trial team).

Following participant consent, the practice will be randomised to intervention (AF screening) or control at a ratio of 1:2. Consented participants in intervention practices will be invited to take part in screening for atrial fibrillation. They will be sent an additional PIS about the screening process and its potential benefits and harms – consistent with a national screening programme leaflet. This invitation needs to be separate from the main research trial invitation as the researchers need to be able to specifically test a screening invitation leaflet of the type (in terms of content, language and tone) that would be used in an NHS national screening programme. Conflating the two information leaflets would make this impossible.

The researchers may also use SMS messages from the practice as part of the recruitment process. This method of communication is increasingly commonly used by practices for communication about routine care in patients in this age group with a great deal of success. It is likely that it would be utilised in national roll-out of an AF screening programme. Some practices may wish to also invite patients to a trial-specific meeting, as part of the invitation to the screening process. Here AF screening is presented and patients are able to ask questions. This approach is used in research practices in the local region to good effect.

During the trial in addition to screening invitation letters, the researchers will also encourage practices to opportunistically approach consented patients, for example at routine appointments, health checks, flu vaccinations, etc. Again, reminder letters and/or emails/SMS will be used if necessary. Procedures at individual practices will be adapted to fit existing practice systems as much as possible, to minimise burden and replicate the delivery of a national screening programme. As a critical factor to the success of the trial, response rates will be closely monitored throughout and approaches and processes changed as required to optimise uptake.

Some participants will also be invited at various points in the screening process to take part in additional, optional qualitative interviews. The initial trial invitation PIS will introduce these elements stating that additional information will be provided at the point of invitation to these elements, and the participant is free to decide at that point whether to take part or not. A decision not to take part will not affect their participation in the main trial. The researchers will carefully sample participants for an invitation to take part in these elements to ensure that they are not overburdened by invitations to participate in multiple qualitative aspects. Please see the qualitative section towards the end of this question for more details of these components.

The screening will be carried out in two stages: an index ECG recorded at the practice, followed by 3 weeks of intermittent screening at home.

The AF screening visit will be with an appropriately trained member of staff, either from the practice or a research nurse from the Clinical Research Network. Participants will be asked to confirm verbal consent to participate in the screening process. The member of staff will assign a single-lead ECG recorder (provided by Zenicor, a Swedish commercial partner in the trial) to the patient and instruct them how to use it. Each ECG records for 30 seconds. Initial screen: an index ECG recording will be performed by the member of staff who will check it using the online system for quality and heart rate. The individual viewing the index ECG trace will not have access to the analysis and resulting classification provided by the system algorithm, and will not be instructed to review the trace in a diagnostic capacity. Further participant instruction and repeat index ECGs will be made if the participant is not able to record an ECG trace of sufficient quality, or if other issues are identified. In a small percentage (about 1%) of individuals it will not be possible to obtain a single lead ECG trace of sufficient quality, purely for physiological reasons. In such a situation (and if the participant is unable to record a good quality trace at the visit) the member of staff will be instructed to take the pulse manually. If the pulse is regular the participant will not undergo further ECG screening as part of the trial, but will remain in the trial for the purposes of data collection. If the pulse is irregular, the participant will leave the trial AF screening process and be managed as per local clinical practice, most likely with a 12 lead ECG. They will not undergo further ECG screening as part of the trial but will remain in the trial for the purposes of data collection. If the heart rate of the index ECG is outside a pre-defined range, the member of staff will be instructed to follow the routine clinical pathway for such patients. The heart rate check will facilitate the early detection of conditions such as fast AF, atrial flutter, supraventricular tachycardia or complete heart block of a degree which may possibly require clinical review in a more timely manner than the routine screening pathway. The patient will remain on the trial AF screening pathway at the discretion of the GP.

Some practices may wish to train participants to use the ECG recorders at group sessions at the practice, both as well as or instead of individual training by the member of staff at the AF screening visit. This approach is reported to work well in other studies. The researchers will monitor patients who attend such groups to determine if it confers additional compliance, and if so, may encourage it in subsequent practices.

Intermittent screening: The participant will be sent home with the ECG recorder and instructions for use. The participant will be asked to take ECG recordings and to transmit each ECG recording to a remote database (via the mobile phone network) by pressing a button on the recorder. In the STROKESTOP trial, sufficient adherence (at least 15 ECG traces) was achieved by 99% of participants (aged 75). Observations from the SAFER feasibility study suggest excellent adherence to 4 ECGs per day across age groups.

The researchers will request ECG traces are recorded 4 times per day (plus when symptomatic) for 3 weeks. They will continue to monitor compliance, problems, ECG quality, incidence of AF

etc. As a result they may revise the frequency and/or duration to achieve the optimal combination. In order to maximise adherence to ECG recording they may intervene by contacting the participant if fewer than the expected number of ECG traces are received (e.g. less than 50%), if the Zenicor system alerts that no ECGs have been received from a device for a certain number of days, or if a significant proportion of poor quality traces are recorded.

When participants start their screening period the researchers will send an email (submitted for review) reiterating good ECG recording technique including the link to the patient ECG recording instruction video on the trial website (previously seen by the committee as part of the feasibility study). This is to try and ensure good quality traces are recorded in order to facilitate review and diagnosis by the cardiologists.

Participants will be asked to return the ECG recorder to the practice at the end of the screening period. Practices will use various means of return, for example in person or by post, or offering specific return appointments, adapting the approach as the trial progresses to ensure optimal ease of return for the participant whilst minimising recorder loss (as they are expensive to replace).

ECG reading system:
The ECG traces are not displayed on the recorder, but are transmitted via mobile signal to a central secure Zenicor database from where they are viewed via a web-based platform. At the end of the screening period when the ECG recorder is returned to the practice, the patient will be flagged on the system as complete and ready for review. The system algorithm classifies and tags each ECG trace as 'no tag', 'possible AF', 'other deviations' or 'poor quality'. ECGs tagged as 'possible AF' or 'other deviations' will be reviewed by a first filter (an experienced cardiac technician or similar) who will forward suspected cases of AF or other abnormalities to a trial cardiologist to confirm if AF or any other important rhythm disturbance is present. The researchers will not require a 12-lead ECG to be undertaken, as single lead ECGs read by cardiologists have high accuracy. If at the end of screening the cardiologist is unable to determine a diagnosis a further assessment may be offered using a different modality (e.g. ECG patch). The details of these patches are still to be confirmed and will be submitted in a future amendment. Review and subsequent classification of ECGs, including diagnosis and additional information for the GP occurs within the web-based platform.

Screening results:
The trial team will log into the Zenicor system to retrieve the diagnostic information of all patients and send it to the practice. The practice will record the information on the patient medical notes. In addition, a full report including cardiologist diagnosis, comments and a copy of relevant ECG traces will be sent to the practice for each patient with a positive (AF or other) diagnosis. The GP will also be provided with access to the Zenicor online system to view and download the ECG traces and reports for all their patients taking part, should they wish to do so. An expedited results pathway will be available for any screening results the cardiologist identifies as clinically urgent. All participants with cardiologist confirmed AF (or other non-AF clinically significant finding) will be notified of their screening result. The researchers will encourage the practice to inform all participants of their screening result following their local process for informing patients of test results. Participants are informed that the results of the screening will be made available to their practice within 8-12 weeks from the date they return the ECG recorder to the practice. This timescale is in line with current NHS screening programmes.

Management of participants with AF:
Participants with confirmed AF will be invited to attend an appointment with the GP (or other

healthcare professional in accordance with local policies) to discuss the diagnosis and the appropriate management including initiation of anticoagulation therapy.

Incidental cardiac findings:
The algorithm that interrogates each ECG trace can also detect and report other rhythm abnormalities in addition to AF. Such ECGs will be reviewed by a cardiologist and reported to the GP via the same process as diagnoses of AF outlined above if they are clinically relevant. The report will recommend to the GP if any further action is necessary, including possible referral. The PIS makes it clear to participants that other (non-AF) rhythm abnormalities may be detected as a result of screening.

This completes the participant involvement in the screening process. Baseline and follow-up data from the GP medical record will be collected in accordance with the consent provided.

Questionnaires – a random sample of patients (1,800; 1,500 invited to screening and 300 not invited to screening, matched for age, sex and postcode deprivation score where possible) will be assessed by postal questionnaire at baseline (pre-invitation) and post-invitation (8 weeks and 6 months). Participants will be sent the questionnaire (consisting of 3 validated measures to assess psychological and functional status) with a covering letter and freepost envelope. Consent will be assumed by completion and return.

Qualitative components:
In addition to the screening process outlined above a small number of patients will also be invited to participate in one or more qualitative components of the trial. The qualitative components of this programme of work will explore how screening is implemented at a practice level, and examine in some detail how practice staff and patients experience the AF screening intervention. Understanding the necessary and sufficient conditions for increased detection of AF and increased use of anticoagulation for screen-detected cases is essential in developing a feasible and sustainable screening programme, both within the main trial and nationally. These activities will be conducted in a small sub-sample of screening practices.

Interviews – participants from various stages of the trial will be invited by the trial team to take part in interviews, either by telephone or face-to-face. These may be one-off interviews (patients who decline the offer of taking part in the trial but agree to speak to a researcher about their reasons, and participants who decline the offer of screening), longitudinal interviews (following individual participants through the screening process with up to 4 interviews, the initial interview face-to-face with subsequent interviews conducted by telephone) or graphic elicitation interviews (interviewees will be supported by the interviewer to complete relational and/or sequential diagrams outlining their medical history, the meaning and implications of an AF diagnosis within this history, and the potential impact of anticoagulation on their daily medication regimens). Interviews will be audio recorded. Please see A30-1 for more details on the consent approach for interviews.

Observations - ethnographic observations of relevant practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. These will result in the observation of patients.

2. Practice staff
Interviews – the trial team will identify staff involved in the delivery of screening at the practice and approach them directly with an invitation to take part in an interview. Interviews will be

conducted with GPs, nurses, practice managers, receptionists, other administrative staff, involved in the delivery of the screening programme to explore reactions to and attitudes towards the various components of the trial AF screening process. Interviews may be repeated as the delivery of the AF screening programme progresses.

Ethnographic observations - ethnographic observations of relevant practice meetings and other practice procedures, alongside repeated visits to observe the day-to-day workings of the practice (including time spent in reception, waiting rooms, administrative offices, and patient consultations (if appropriate)), to inform understanding of the context within which the screening programme is being delivered. No photos or videos will be taken. Field notes will not include any identifiable information.

3. External stakeholders
Part of the practice case studies interview work may involve identifying relevant external stakeholders to the practice and inviting them to take part in an interview. These individuals may include local care commissioners, clinical pharmacists, training providers, for example. Interviews may be repeated as the delivery of the AF screening programme progresses.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 04/07/2023:
Stroke incidence, defined as stroke of any severity but excluding transient ischaemic attack. Ischaemic and haemorrhagic stroke will be combined. Collection of stroke incidence will be via electronic health registries (including HES, ONS and SSNAP) and GP medical records, approximately annually for an average of 4 years.

Previous primary outcome measure:
Stroke incidence, defined as stroke of any severity but excluding transient ischaemic attack. Ischaemic and haemorrhagic stroke will be combined. Collection of stroke incidence will be via electronic health registries (including HES, ONS and SSNAP) and GP medical records, approximately annually for an average of 5 years.

Key secondary outcome(s))
Current secondary outcome measures as of 08/01/2024 to 04/07/2023:
Collected via electronic health registries (including HES, ONS, MiNAP and SSNAP) and GP medical records, for an average of 4 years:
1. Bleeding episode requiring hospital admission (including haemorrhagic stroke, to be reported separately)
2. Myocardial infarction; ischaemic stroke
3. Cardiovascular events (myocardial infarction + stroke + other admissions for cardiovascular disease – including heart failure)
4. All-cause mortality
5. Cardiovascular mortality
6. Dementia
7. AF detection rates
8. Anticoagulation rates
9. New diagnoses of depression and anxiety
10. Psychological effects of screening and impact on functional status assessed using the Spielberger state trait anxiety inventory (STAI), EQ5-D and Short-form 8 (SF-8) questionnaire

posted to a random sample of participants in intervention and control practices at baseline and post-invitation to the trial (pilot trial only)

Previous secondary outcome measures as of 04/07/2023:
Collected via electronic health registries (including HES, ONS, MiNAP and SSNAP) and GP medical records, approximately annually for an average of 4 years:
1. Bleeding episode requiring hospital admission
2. Myocardial infarction
3. Cardiovascular events (myocardial infarction + stroke + other admissions for cardiovascular disease – including heart failure)
4. All-cause mortality
5. Cardiovascular mortality
6. Dementia
7. AF detection rates
8. Anticoagulation rates
9. New diagnoses of depression and anxiety
10. Psychological effects of screening and impact on functional status assessed using the Spielberger state trait anxiety inventory (STAI), EQ5-D and Short-form 8 (SF-8) questionnaire posted to a random sample of participants in intervention and control practices at baseline and post-invitation to the trial

Previous secondary outcome measures:
Collected via electronic health registries (including HES, ONS, MiNAP and SSNAP) and GP medical records, approximately annually for an average of 5 years:
1. Bleeding episode requiring hospital admission
2. Myocardial infarction
3. Cardiovascular events (myocardial infarction + stroke + other admissions for cardiovascular disease – including heart failure)
4. All-cause mortality
5. Cardiovascular mortality
6. Dementia
7. AF detection rates
8. Anticoagulation rates
9. New diagnoses of depression and anxiety
10. Psychological effects of screening and impact on functional status assessed using the Spielberger state trait anxiety inventory (STAI), EQ5-D and Short-form 8 (SF-8) questionnaire posted to a random sample of participants in intervention and control practices at baseline and post-invitation to the trial

Completion date
30/09/2028

Eligibility

Key inclusion criteria
1. Have given informed consent to participate
2. Be aged 70 years or over

Participant type(s)
All

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
70 years

Sex
All

Total final enrolment
89575

Key exclusion criteria
Current exclusion criteria as of 08/01/2024 to 25/07/2022:
1. On anticoagulation therapy
2. On the practice palliative care register
3. Resident in a nursing or care or residential home
4. Consented to another trial that will affect participation in SAFER
5. Non-UK resident

Previous exclusion criteria as of 25/07/2022:
1. On long-term anticoagulation therapy
2. On the practice palliative care register
3. Resident in a nursing or care or residential home
4. Consented to another trial that will affect participation in SAFER
5. Non-UK resident

Previous exclusion criteria:
1. Long-term anticoagulation therapy for stroke prevention
2. On the palliative care register
3. Resident in a nursing/care/residential home

Date of first enrolment
01/04/2020

Date of final enrolment
31/01/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR CRN: Eastern
United Kingdom
NR1 1QQ

Study participating centre
NIHR CRN: North East and North Cumbria
United Kingdom
NE3 3HD

Study participating centre
NIHR CRN: North West Coast
United Kingdom
L7 8XP

Study participating centre
NIHR CRN: Yorkshire and Humber
United Kingdom
S10 2SB

Study participating centre
NIHR CRN: Greater Manchester
United Kingdom
M13 9WL

Study participating centre
NIHR CRN: East Midlands
United Kingdom
LE1 5WW

Study participating centre
NIHR CRN: West Midlands
United Kingdom
CV3 2TX

Study participating centre
NIHR CRN: West of England
United Kingdom
BS1 2NT

Study participating centre
NIHR CRN: Thames Valley and South Midlands
United Kingdom
OX3 9DU

Study participating centre
NIHR CRN: Kent, Surrey and Sussex
United Kingdom
ME8 0NZ

Study participating centre
NIHR CRN: Wessex
United Kingdom
SO30 2UN

Study participating centre
NIHR CRN: South West Peninsula
United Kingdom
PL6 8BX

Study participating centre
NIHR CRN: North Thames
United Kingdom
W1T 7HA

Study participating centre
NIHR CRN: South London
United Kingdom
SE1 9RT

Study participating centre
NIHR CRN: North West London
United Kingdom
W12 0HT

Sponsor information

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Organisation
NHS Cambridgeshire & Peterborough Integrated Care Board (ICB)

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: RP-PG-0217-20007

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

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	Pilot	09/09/2022	24/01/2023	Yes	No
Protocol article	Main study	25/04/2025	02/05/2024	Yes	No
HRA research summary			28/06/2023	No	No

Study website	Study website	11/11/2025	11/11/2025	No	Yes