The SAFER programme

Screening for **A**trial **F**ibrillation with **E**CG to Reduce stroke

Munich, 25th August 2018

Funding

- National Institute of Health Research (NIHR) Programme Grant for Applied Research
- NIHR National School for Primary Care Research – additional feasibility work
- Wellcome Trust Clinical Doctoral Fellowship – feasibility issues

Research question: Is screening for atrial fibrillation (AF) effective and cost effective in reducing stroke?

Objectives of NIHR Programme:

- Test feasibility of a screening programme (including paroxysmal AF) set in general practice in people aged 65 and over using a hand-held ECG recorder (Zenicor)
- Carry out an internal pilot trial
- Perform a cluster randomised controlled trial with primary outcome of stroke incidence
- Perform parallel qualitative studies to inform how screening can be optimised in both the main trial and if implemented nationally
- Use economic modelling to determine whether, in the light of the trial results, screening is cost-effective

Initial Screening Process

TARGET POPULATION

-aged 65 and over: upper and lower age limit for trial will depend on feasibility work

-people with AF label not on anticoagulation are eligible

EXCLUSION

-long term anticoagulation

-palliative care register

-nursing home resident

Screening approach

- Single lead ECG using Zenicor device
- 30 second screen, followed by 2 weeks of intermittent screening twice daily for 30 secs. (length and frequency may change from feasibility)
- Positive ECGs will be read by a study cardiologist
- Confirmed positives: patient will see GP to discuss anticoagulation
- Approach to participants: different methods will be employed during feasibility study
- Staff training: how to carry out screening from organisational perspective; how to use hand-held device; role of anticoagulation in stroke prevention
- Organisational approach to Quality Assurance

Approaches to patients

- Initial invitation to contact practice
- Practice sends screening appointments
- Repeat invitation towards end of screening
- Opportunistic, followed by clinic appointment (which could be done as a group session)
- More?

Patient consent

- Two stage:
  - Consent for follow up of health care records
  - Information about screening – verbal consent

Feasibility study

Objectives:	Phase 1: 1. Determine how long and how often people should be screened to see if they do have paroxysmal AF 2. Determine the practice experience of AF screening (this continues into phase 2) 3. Determine the patient experience of AF screening Phase 2: 1. Determine if screening for AF (including paroxysmal AF) is feasible in general practice in people aged 65 and over using a hand-held electrocardiogram (ECG) recorder (Zenicor) 2. Develop a process of audit, feedback and quality assurance of screening to inform our fidelity assurance in the subsequent trial 3. Finalise target population age range for the cluster randomised trial

Outcome Measures	Phase 1: 1. Incremental increase in new AF detection rate by number of days screened and by number of times screened per day 2. New AF detection rate 3. % of new AF detected that is persistent versus paroxysmal 4. % of patients with an AF code on the GP record who have confirmed AF from the screening process

+ develop systems of quality assurance

Feasibility Outcomes (2)

Phase 2:

1. % eligible patients who consent – estimated to be around 50%
2. % people who consent who are screened in six months – estimated to be around 40% over six months
3. % people screened who have 2-week paroxysmal AF screening
4. % people whose paroxysmal AF screening includes at least 15 ECG traces

Feasibility Outcomes (3)

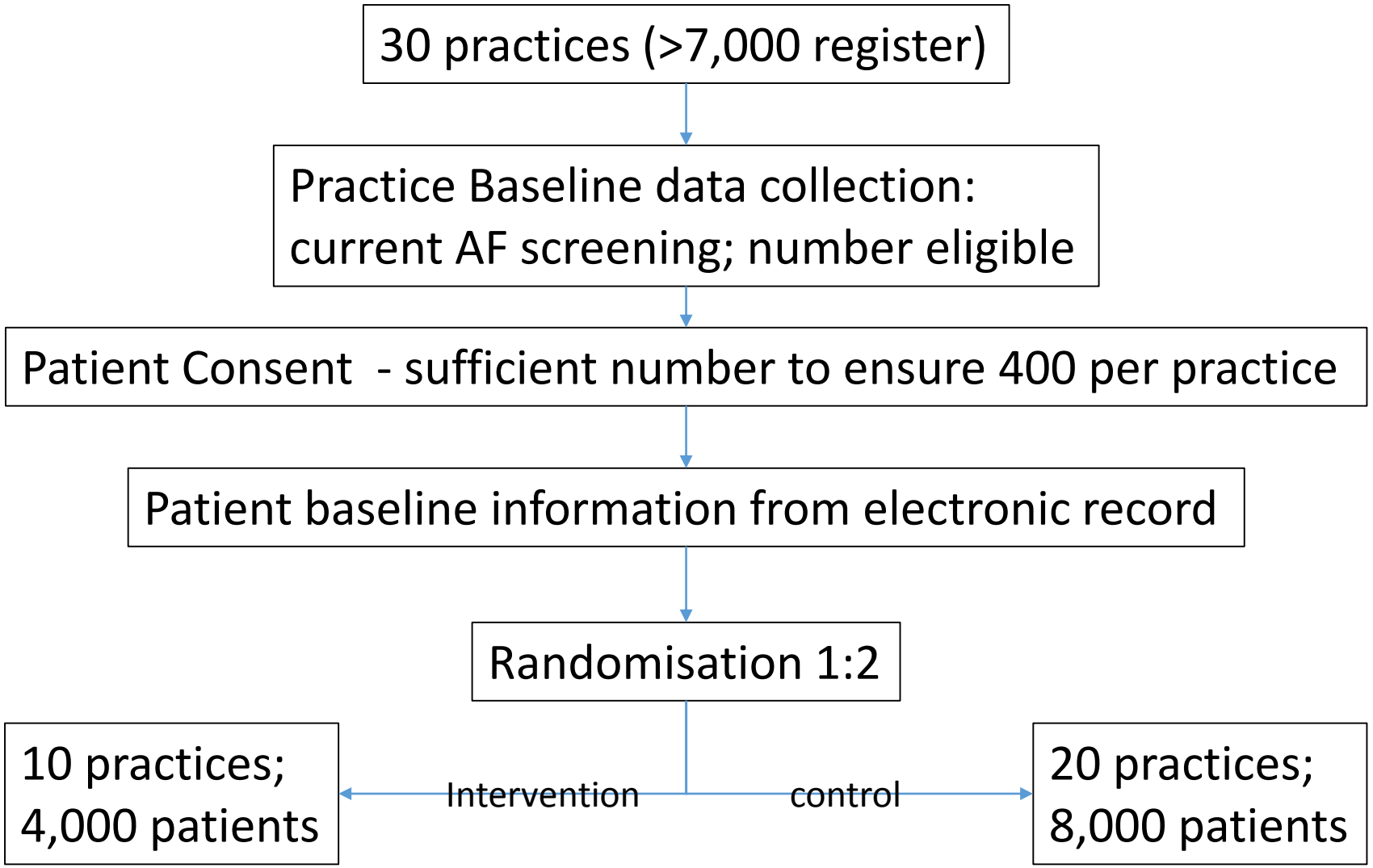
5. % people who have AF identified (subdivided by new/previously known; paroxysmal/permanent)
6. % people who have AF identified who are reviewed by their GP
7. % people with AF commenced on anticoagulation (sub-divided by new/previously known; CHA2DS2-Vasc score: 1 or ≥1)
8. % completeness of baseline data from electronic record
9. Report all the above criteria in age sub-groups to refine age entry criteria to the internal pilot.

Internal Pilot Trial

OBJECTIVES

- Determine whether key parameters (rate of AF detection; uptake of anticoagulation in screen positive confirmed AF) achieved to inform trial progression
- Inform power calculation for main trial
- Inform further iteration of screening procedures
- Quantify psychological harms from screening
- Pilot procedures for main trial

Internal Pilot: current design



Internal Pilot: Follow up

- Postal questionnaire (a sample; quality of life & consequences of screening)
- At one year:
  - Electronic GP records: AF diagnoses and anticoagulation
  - Zenicor database: number screened; number cases AF identified;
- Long term:
  - NHS digital: mortality; Hospital Episode Statistics
  - Stroke and Myocardial Infarction National Audits (SSNAP; MINAP): long term clinical events
  - Electronic GP records: long term clinical events

PROGRESSION TO END POINT POWERED TRIAL

We do not propose rigid stop/go criteria. The key issue is whether the results of the internal pilot suggest that the end point powered trial will detect a significant effect. We will re-run the power calculation in the light of the internal pilot data to determine whether or not a trial is worth continuing. We believe that it would be feasible to expand recruitment if indicated, but recognise this would require a decision from NIHR as to whether funding an expanded trial would offer value for money.

We will evaluate any evidence of psychological harm emerging from our internal pilot against indicative evidence of the expected beneficial effect (e.g. AF detection, anticoagulation uptake) or if measures could be introduced to mitigate such harm. At this point, we will use the data from the pilot study to update the Welton model. The model results will be used to inform the decision as to whether or not the study should proceed.

Therefore, we propose a formal review is undertaken at the end of the internal pilot in consultation with the NSC to consider whether or not to proceed to the end-point trial.

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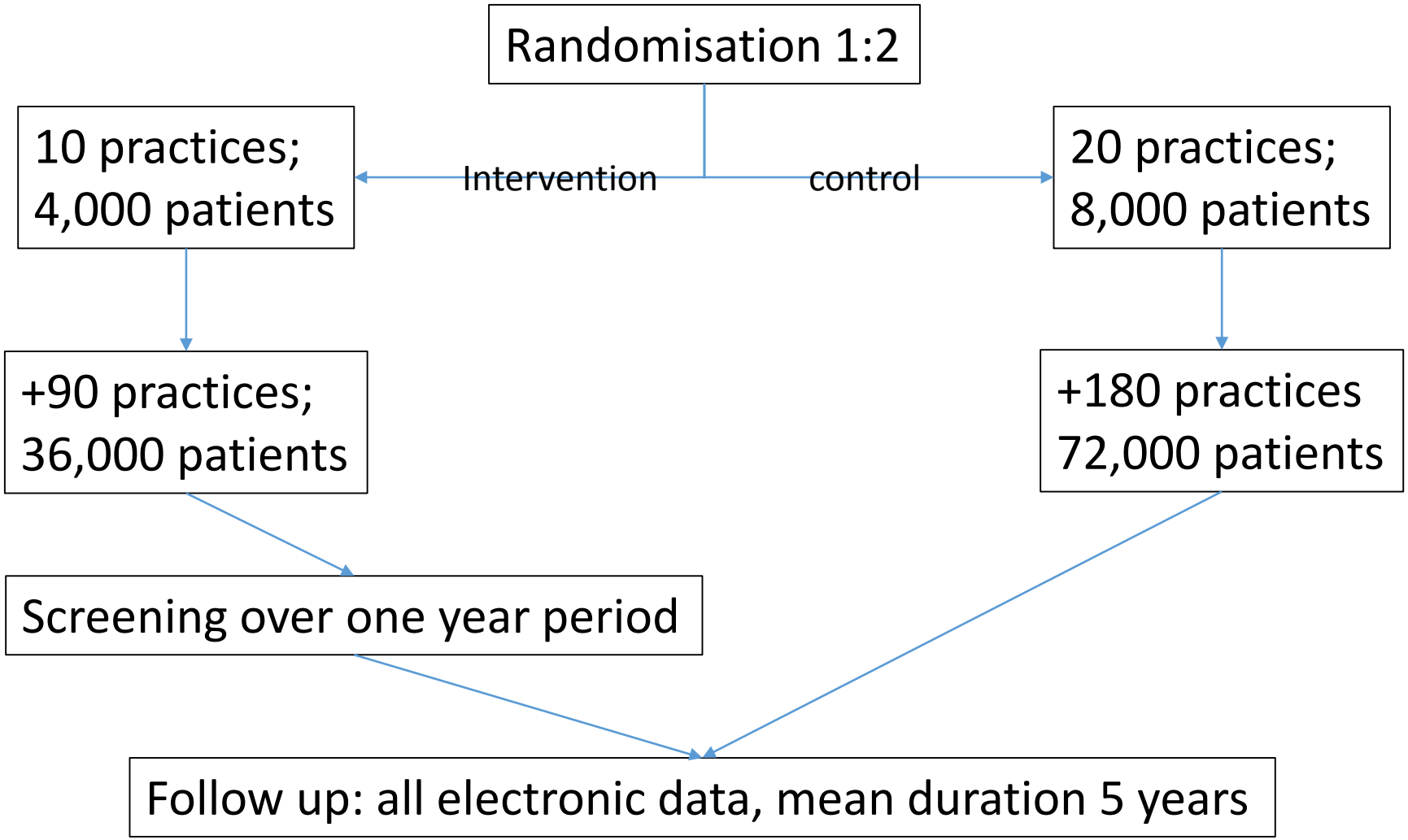
1. Does the updated power calculation suggest a feasible trial?
2. Does the updated economic model suggest that benefit is very unlikely?

End point powered trial



Outcome measures

- Primary: Stroke incidence
- Secondary:
  - All cause mortality
  - Bleeding episode requiring hospital admission
  - Myocardial infarction
  - Cardiovascular events (MI + stroke + other admissions for cardiovascular disease including heart failure + cardiovascular death)
  - Cardiovascular mortality
  - Dementia
  - Depression & anxiety
  - AF
  - Anticoagulation rates (in AF)

Sources of outcome data

- GP electronic data (end of study)
  - AF; anticoagulation; dementia; stroke; MI; other cardiovascular diseases; anxiety & depression
- NHS digital
  - Deaths
  - HES: bleeding episodes; strokes ; MI; other cardiovascular admissions
  - Stroke Sentinel National Audit Project: strokes
  - Myocardial National Audit Project: myocardial infarction

Timetable – current targets

- Feasibility study
  - Phase 1: completed by July 2019
  - Phase 2: completed by October 2019
- Internal Pilot
  - Completed screening in 10 pilot practices by October 2020
  - Decision made on progression to main trial during 2021
- Main trial
  - Completed AF screening in 100 practices during 2023
  - Completed follow up during 2026