Accepted Manuscript online: 2026-01-15 Article published online: 2026-01-30

Invited Clinical Focus

SAFER: A Programme of Research to Determine if Intermittent Single-Lead ECG Screening for Atrial Fibrillation Reduces the Risk of Stroke

Jonathan Mant[1], Andrew Dymond[1], Kate Williams[1] on behalf of the SAFER Investigators[‡]

Affiliation addresses are listed at the end of the article.

ABSTRACT

This article describes the SAFER (Screening for Atrial Fibrillation with ECG to Reduce stroke) programme that was established to determine whether intermittent screening for atrial fibrillation with a single-lead electrocardiogram reduces the risk of stroke and other key outcomes such as death, dementia and cardiovascular disease. The programme comprises feasibility studies, a pilot trial, a randomised controlled trial, qualitative studies and an economic analysis. Recruitment and screening for the trial have been completed, and it is anticipated that follow-up will finish in 2027.

Keywords atrial fibrillation, stroke prevention, screening

received October 23, 2025 | **accepted after revision** December 29, 2025 | **accepted manuscript online** January 15, 2026 | **article published online** 2026

Bibliography Thromb Haemost **DOI** 10.1055/a-2780-0387 **Art ID** TH-25-10-0579

‡ The details of the SAFER Investigators are given in the **Supplementary Appendix** (available in the online version only).

Correspondence Jonathan Mant, MD, Department of Public Health and Primary Care, Primary Care Unit, University of Cambridge, Cambridge, United Kingdom, Email: jm677@medschl.cam.ac.uk

Introduction

Atrial fibrillation (AF) is the commonest cardiac arrhythmia. It is often asymptomatic and is associated with a major increase in risk of stroke that can be substantially reduced by treatment with anticoagulation. However, there is insufficient evidence to determine whether the potential benefits of screening for AF outweigh potential harms.[1] While there are some differences in international guidelines (**Table 1**), they are consistent in acknowledging that more evidence would be helpful. Therefore, we established the SAFER (Screening for Atrial Fibrillation with ECG to Reduce stroke) programme to answer the question as to whether screening for AF reduces risk of stroke and other key outcomes such as death, dementia and cardiovascular disease and whether these benefits would outweigh the major potential harm (increased bleeding risk through anticoagulation treatment).

There are many ways to screen for AF.[2] Since recent trials have not shown that single time point screening detects more AF than usual care, perhaps because such an approach is effectively current practice,[3] we opted to evaluate a more intensive approach to screening that would detect paroxysmal AF.[4] Recognising that stroke risk in AF is related to AF burden (i.e. the frequency and duration of AF episodes) in paroxysmal AF and that therefore it maybe that not all AF that is identified warrants treatment with anticoagulation,[5] we opted to evaluate intermittent use of a single-lead handheld electrocardiogram (ECG) rather than more intensive methods of monitoring. Previous trials that have examined the impact of prolonged screening for AF on cardiovascular outcomes are summarised in **Table 2**. None of the trials were of sufficient size to give a definitive answer, though collectively they suggest that there might be a benefit.[6]

Our programme has the following methods and objectives:

1. To carry out feasibility studies to determine whether a screening programme set in primary care using a handheld ECG device is feasible.
2. To perform a pilot trial to determine whether key parameters (rate of AF detection; uptake of anticoagulation in people identified with AF) are achieved, and to quantify any psychological harms from screening.
3. To perform a randomised controlled trial (RCT) to evaluate whether screening for AF reduces stroke incidence.
4. To perform parallel qualitative studies to inform how screening can be optimised.
5. To use economic modelling to determine whether screening is cost-effective.

The relationship between these studies and their timelines is shown in **Fig. 1**. Here, we report our progress with the programme and our initial findings.

Feasibility Studies

Feasibility studies were carried out between 2019 and 2021.[7] We had originally intended to start the pilot trial at the beginning of

Table 1 International guidelines' recommendations on screening for atrial fibrillation

U.S. Preventive Services Taskforce[1]	**Current evidence is insufficient** to assess the balance of benefits and harms of screening for AF
United Kingdom National Screening Committee[20]	**Screening is not recommended** because ▪ There are different types of AF, and it is not clear if all of these have the same risk for stroke ▪ It is not known how effective treatment for AF is in people found through screening ▪ It is not known if screening is more beneficial for people with AF than the current approach to detection and management
European Society of Cardiology[21]	**Routine heart rhythm assessment during healthcare contact is recommended** in people aged 65 and over for AF detection **Population-based screening for AF using a prolonged non-invasive ECG-based approach should be considered** in people aged 75 or over, or 65 and over with additional risk factors
Asia Pacific Heart Rhythm Society[22]	**Opportunistic screening for AF is recommended** for people aged 65 and over **Systematic screening may be considered** to detect AF in people aged 75 or over or those at high stroke risk

Abbreviations: AF, atrial fibrillation; ECG, electrocardiogram.

Table 2 Trials of prolonged screening for atrial fibrillation with a cardiovascular end point ordered by study size

Study	Study size and average age (years)	Screening method	Clinical end point	Length of follow-up	Clinical outcome: Screening versus control
STROKESTOP[8]	28,768 (76)	2× daily using a handheld ECG for 2 weeks	Composite of stroke, systemic embolus, major bleed, death	Median 6.9 years	5.45 per 100 years versus 5.68 per 100 years, HR 0.96 (95% CI 0.92–1.00)
STROKESTOP II[9]	28,712 (76.5)	Single-lead ECG and NT-proBNP; further intermittent handheld ECG screening for 2 weeks, four times per day if NT-proBNP is ≥125 ng/L	Stroke or systemic embolus	Median 5.1 years	0.99 per 100 years versus 1.03 per 100 years, HR 0.96 (95% CI 0.86–1.06)
GUARD-AF[23]	11,905 (75.8)	ECG patch monitor for 14 days	Stroke	Median 15.3 months	0.55 per 100 years versus 0.50 per 100 years, HR 1.10 (95% CI 0.69–1.75)
AMALFI[24]	5,040 (78)	ECG patch monitor for 14 days	Stroke	2.5 years	2.7% versus 2.5%, RR 1.08 (95% CI 0.76–1.53)
LOOP[5]	6,004 (75)	Implantable loop recorder, median duration 39.3 months	Stroke or systemic embolus	Median 64.5 months	0.88 per 100 years versus 1.09 per 100 years, HR 0.80 (95% CI 0.65–1.05)

Abbreviations: CI, confidence interval; ECG, electrocardiogram; HR, hazard ratio; NT-proBNP, N-terminal pro b-type natriuretic peptide.

2020, but due to the coronavirus disease 2019 (COVID-19) pandemic, we carried out an additional feasibility study looking at remote delivery of the single-lead handheld ECG rather than in-person delivery that we had tested in 2019. Overall, the feasibility studies involved screening 2,429 participants aged 65 and over and 64 (2.6%) cases of AF were identified.

Key Findings

- Screening for AF in primary care using a single-lead handheld ECG device is feasible. Of the people invited to the screening, 88% successfully completed it. This is higher than the other large trials of screening using a single-lead ECG device, STROKESTOP (51.3% uptake) and STROKESTOP II (49.7% uptake), reflecting that consent to take part in the trial was sought prerandomisation in SAFER, whereas in the other studies it was only sought in people randomised to screening. [8,9] Of the people identified to be in AF, 83% of people were commenced on anticoagulation.
- Face-to-face contact to show how to use the single-lead handheld ECG device is not required. Uptake of screening was 87% in people offered face-to-face device delivery and 90% in people sent the device by post. The quality of the ECGs was assessed using a proprietary algorithm. At least 56 interpretable ECGs were provided by 98% of participants following face-to-face initiation of screening, and 97% of participants who received the ECG device by post.
- There is no need to impose an upper age limit on screening. In the 85 years and over age group, AF was detected in 9.2% of participants, anticoagulation uptake was the same as in other age groups, and though there was a slight drop off in terms of ECG quality, 91% of participants did provide at least 56 interpretable ECGs. Agreement to participate drops off at the oldest ages: 23% of people aged 85 and over who were invited took part in the feasibility studies, as compared to 48% of people aged 70 to 74, but the studies demonstrated that for those who do wish to take part in the oldest age group, screening can be performed effectively.

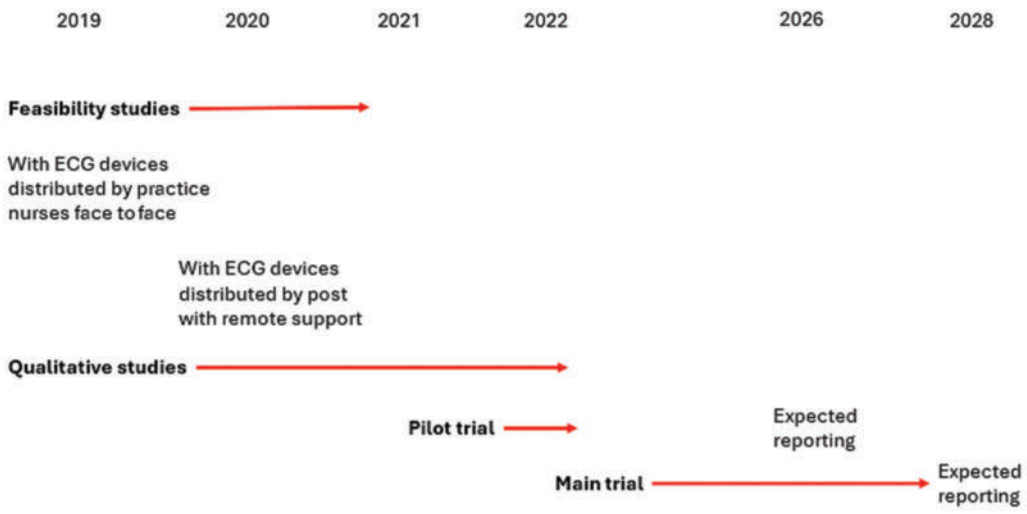

Fig. 1 SAFER studies and timeline. ECG, electrocardiogram; SAFER, Screening for Atrial Fibrillation with ECG to Reduce stroke.

Pilot Trial

The pilot trial was carried out from 2021 to 2022.[10] This was a cluster randomised trial with general practices being the units of randomisation. Thirty-nine practices were randomised, and approximately 14,000 participants aged 70 and over were recruited. The screening process used is illustrated in **Fig. 2**. The key parameters were met in terms of uptake of screening, detection of AF, and uptake of anticoagulation in people detected with AF. Our comparison of AF detection rates at 1 year in the intervention and control arms and our comparison of quality of life in these groups will be reported in 2026.

Randomised Controlled Trial

Recruitment to the main RCT took place from 2021 to 2024, with screening finishing in early 2025. The design of the trial is shown in **Fig. 3**.[4] Randomisation is by household to avoid contamination. The primary outcome is stroke (ischaemic and haemorrhagic combined). In addition to the outcomes shown in the figure, process data such as the use of anticoagulation will be collected. The same screening process was used as shown in **Fig. 2**. Recruitment targets were exceeded with around 89,000 people randomised. Follow-up is via electronic health records and is anticipated to finish in 2027. We hope to report the results in 2028, including our analysis of the cost-effectiveness of screening.

Qualitative Findings

Extensive qualitative work accompanied the early stages of the programme.[11] This influenced many aspects of how the screening was delivered, including, for example, the importance of informing all participants of their screening result, regardless of whether it required any action. It provided insights into why some people

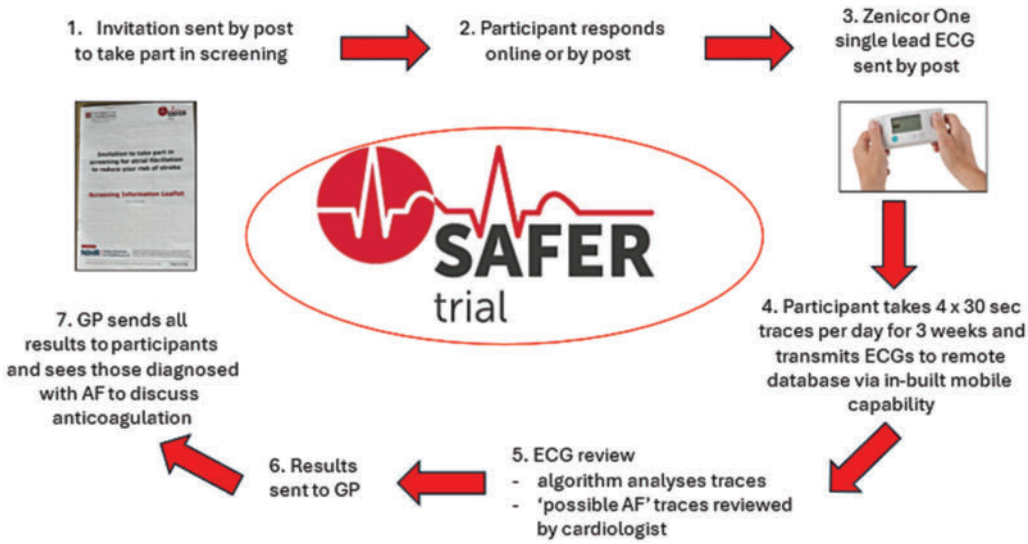

Fig. 2 Screening process in SAFER. ECG, electrocardiogram; SAFER, Screening for Atrial Fibrillation with ECG to Reduce stroke. GP, General Practitioner.

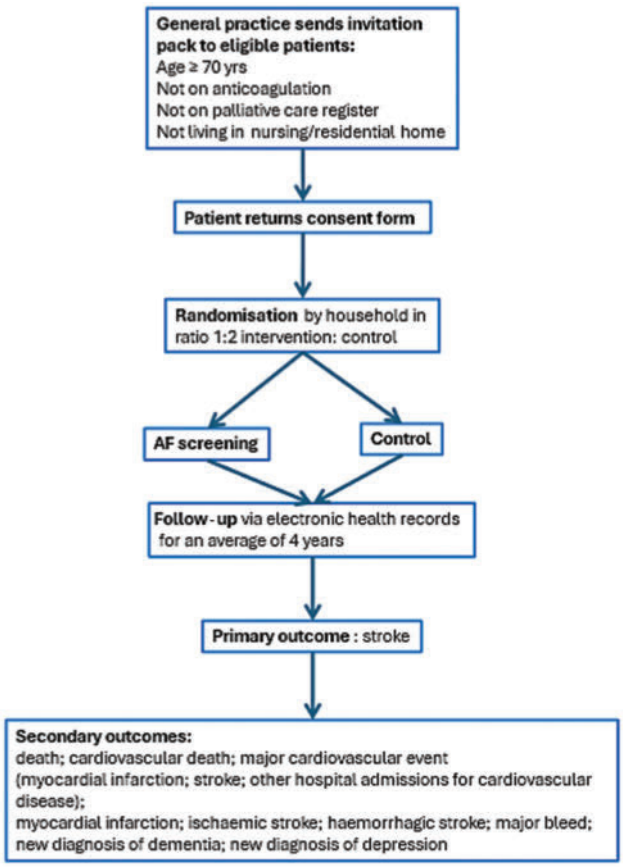

Fig. 3 Outline of design of the SAFER RCT. AF, atrial fibrillation; RCT, randomised controlled trial; SAFER, Screening for Atrial Fibrillation with ECG to Reduce stroke; yrs, years.

did not want to take part in screening, a major factor being doubts about its utility at their age.[12] Conversely, we also found that many people were highly motivated to take part in screening, even though they might not understand much about AF. People did not perceive there to be major harms from such screening.[13]

Lessons Learned: How to Implement Screening for Atrial Fibrillation

While conducting the SAFER programme, we have gained insight into how a screening programme might be conducted.

Role of Primary Care

When the programme was initiated, we had assumed that primary care would be at its core. The COVID-19 pandemic made that impractical, and we found that remote delivery of the screening was an acceptable way to perform it. During the feasibility phase, we did explore whether this remote delivery might be better coordinated by primary care. However, we found no important advantages to this over administrator-led screening outside of general practice.[14] Therefore, given that primary care remains under considerable pressure, it would seem appropriate to coordinate the screening outside of primary care. That said, in our programme, the local general practice was responsible for sending out the initial trial invitations, informing patients of their results and then initiating anticoagulation where appropriate.

Importance of Electrocardiogram Quality

We found that the reliability of reading single-lead ECGs was only moderate.[15] An important determinant of the reliability was the quality of the ECGs. Therefore, we recommended in the trial phase that poor quality ECGs (as identified by the algorithm) were ignored. Participants received written instructions on how to use the ECGs and were offered a telephone call as well (which a few took up). We investigated whether supplementary telephone training of participants would lead to an improvement in ECG quality, but this was not the case.[16] Indeed, we found that most participants provided an adequate number of reasonable quality ECGs, and the proportion of reasonable quality ECGs improved over the course of the 3 weeks that participants undertook screening. This suggests that a minimum screening period should be introduced for this approach to AF screening.

Choice of Electrocardiogram Modality for Screening

In terms of ECG modality for longer-term screening for AF, trials have been published using both continuous patch ECG and intermittent single-lead ECG (see **Table 2**). When SAFER and NORSCREEN[17] have been published, there will be large numbers of patients included in trials of both approaches. Currently, it is difficult to choose between the two approaches. Continuous monitoring using a patch is likely to produce better quality ECGs than single-lead intermittent monitoring, but conversely, is likely to detect more incidental findings that might need action and more cases of AF that might not need anticoagulation.

Conclusion

Current evidence from RCTs is insufficient to determine whether prolonged screening should be undertaken for AF. Factors contributing to this include the insufficient size of the trials and low uptake of screening.[18] The SAFER trial has overcome these limitations and will clarify the answer to this question. It is an important question to answer, as the potential gains, not only in improved health but also in reduced resource use in health care, are substantial.[19] The position of the United Kingdom National Screening Committee is to 'await the conclusion of the SAFER trial' before its next review of the evidence.[20]

Author Affiliation

1 Department of Public Health and Primary Care, Primary Care Unit, University of Cambridge, Cambridge, United Kingdom

Statements and Additional Information

Conflict of Interest J.M. has performed consultancy work for BMS/Prizer and Omron. The other authors declare that they have no conflict of interest.

Acknowledgements We acknowledge the support of the Independent Programme Steering Committee: Professor Christian Mallen, University of Keele (chair); Professor Anthony Rudd, King's College London (independent member); Professor Ann Marie Swart, University of East Anglia (independent member); Professor Andy Vail, University of Manchester (independent member); and Dr Bob Ward (independent lay member).

Funding Information The SAFER programme is funded by the National Institute for Health and Care Research (NIHR) Programme Grants for Applied Research (RP-PG-0217-20007). SAFER is a contributor to/partner of AFFECT-EU, receiving funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement number 847770. The NIHR School for Primary Care Research (SPCR-2014-10043, project 410) funded parts of the feasibility study. This work was supported by core funding from the NIHR Cambridge Biomedical Research Centre (NIHR203312). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the United Kingdom Department of Health and Social Care.

Clinical Trial Registration ISRCTN72104369

Supplementary Material is available at https://doi.org/10.1055/a-2780-0387.

References

1 Davidson KW, Barry MJ, Mangione CM, et al; US Preventive Services Task Force. Screening for Atrial Fibrillation: US Preventive Services Task Force Recommendation Statement. JAMA 2022;327(04):360–367

2 Brandes A, Stavrakis S, Freedman B, et al. Consumer-led screening for atrial fibrillation: Frontier review of the AF-SCREEN International Collaboration. Circulation 2022;146(19):1461–1474

3 Chao TF, Yeh YH, Chan YH, et al. The report of community-based and government-endorsed screening program of atrial fibrillation in Taiwan. Thromb Haemost 2024;124(01):61–68

4 Mant J, Modi RN, Dymond A, et al; SAFER author group. Randomised controlled trial of population screening for atrial fibrillation in people aged 70 years and over to reduce stroke: Protocol for the SAFER trial. BMJ Open 2024;14(04):e082047

5 Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): A randomised controlled trial. Lancet 2021;398(10310):1507–1516

6 McIntyre WF, Diederichsen SZ, Freedman B, Schnabel RB, Svennberg E, Healey JSon behalf of the SCREEN-AF and AFFECT-EU Investigators. Screening for atrial fibrillation to prevent stroke: A meta-analysis. Eur Heart J Open 2022;2(04):oeac044

7 Mant J, Modi RN, Charlton P, et al. The feasibility of population screening for paroxysmal atrial fibrillation using hand-held electrocardiogram devices. Europace 2024;26(03):1–9

8 Svennberg E, Friberg L, Frykman V, Al-Khalili F, Engdahl J, Rosenqvist M. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): A multicentre, parallel group, unmasked, randomised controlled trial. Lancet 2021;398(10310):1498–1506

9 Kemp Gudmundsdottir K, Svennberg E, Friberg L, et al. Randomised invitation to systematic NT-proBNP and ECG screening in 75 year olds to detect atrial fibrillation: STROKESTOP II. Circulation 2024;150(23):1837–1846

10 Williams K, Modi RN, Dymond A, et al. Cluster randomised controlled trial of screening for atrial fibrillation in people aged 70 years and over to reduce stroke: Protocol for the pilot study for the SAFER trial. BMJ Open 2022;12(09):e065066

11 Powell A, Hoare S, Modi R, et al. How to embed qualitative research in trials: Insights from the feasibility study of the SAFER trial programme. Trials 2022;23(01):394

12 Hoare S, Thomas GPA, Powell A, Armstrong N, Mant J, Burt J. Why do people choose not to take part in screening? Qualitative interview study of atrial fibrillation screening nonparticipation. Health Expect 2023;26(06):2216–2227

13 Hoare S, Powell A, Modi RN, et al; SAFER Authorship Group. Why do people take part in atrial fibrillation screening? Qualitative interview study in English primary care. BMJ Open 2022;12(03):e051703

14 Modi RN, Massou E, Charlton PH, et al. Screening for atrial fibrillation with or without general practice involvement: A controlled study. BMC Prim Care 2025;26(01):185

15 Hibbitt K, Brimicombe J, Cowie MR, et al. Reliability of single-lead electrocardiogram interpretation to detect atrial fibrillation: Insights from the SAFER feasibility study. Europace 2024;26(07):euae181

16 Prathivadi Bhayankaram K, Mant J, Brimicombe J, Dymond A, Williams K, Charlton PH. Telephone training to improve ECG quality in remote screening for atrial fibrillation. Physiol Meas 2024;45(12):125005

17 Boskovic M, Jortveit J, Haraldsen MB, et al. The NORwegian atrial fibrillation self-SCREENing (NORSCREEN) trial: Rationale and design of a randomized controlled trial. Europace 2024;26(10):euae228

18 Lane DA, Andrade JG, Arbelo E, et al. Seminar on atrial fibrillation. Lancet 2026; In press

19 Lyth J, Svennberg E, Bernfort L, et al. Cost-effectiveness of population screening for atrial fibrillation: The STROKESTOP study. Eur Heart J 2023;44(03):196–204

20 GOV.UK. Atrial fibrillation - UK National Screening Committee (UK NSC). Accessed October 8, 2025; available at: https://view-health-screening-recommendations.service.gov.uk/atrial-fibrillation/

21 Van Gelder ICV, Rienstra M, Bunting KV, et al; ESC Scientific Document Group. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2024;45(36):3314–3414

22 Chan N-Y, Orchard J, Agbayani M-J, et al. 2021 Asia Pacific Heart Rhythm Society (APHRS) practice guidance on atrial fibrillation screening. J Arrhythm 2021;38(01):31–49

23 Lopes RD, Atlas SJ, Go AS, et al. Effect of screening for undiagnosed atrial fibrillation on stroke prevention. J Am Coll Cardiol 2024;84(21):2073–2084

24 Wijjesurenda R, Pessoa-Amorim G, Buck G, et al. Remote screening for asymptomatic atrial fibrillation: The AMALFI Randomised Clinical Trial. JAMA 2025;334:1349–1357