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Published in:
International Journal of Cardiology

DOI:
10.1016/j.ijcard.2019.03.062

Publication date:
2019

Document Version
Publisher's PDF, also known as Version of record

International Journal of Cardiology 288 (2019) 94–99

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Atrial fibrillation case finding in over 65 s with cardiovascular risk factors – Results of initial Scottish clinical experience

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ARTICLE INFO

Article history:
Received 16 May 2018
Received in revised form 19 March 2019
Accepted 28 March 2019
Available online 29 March 2019

Keywords:
Atrial fibrillation
Screening
Stroke
Public health
Telehealth
Ambulatory monitoring

ABSTRACT

Background: Atrial fibrillation (AF) is a major preventable risk factor for stroke and may be silent in elderly individuals who are at especially high risk. This paper describes the first phase of implementation of a clinical AF detection programme in a community setting. Objectives were (i) to determine the feasibility of using a handheld ECG recording system for AF detection among individuals aged 65 years or more, who have cardiovascular risk factors. (ii) to estimate the yield of previously undiagnosed atrial fibrillation cases, and the proportion of these who would be suitable for oral anticoagulation.
Methods: a handheld ECG monitor was placed in each of 23 primary care practices across Scotland. Eligible patients attending for annual health checks had ECGs recorded, and the ECGs were transmitted and interpreted by two senior cardiologists. ECG quality was rated, and an adjudication made on the rhythm. For patients confirmed with AF, stroke and bleeding risk were estimated using CHA_2DS_2-VASc and HAS-BLED scoring tools.
Results: single lead ECGs were recorded in 1805 patients (703 female and 1102 male), mean (SD) age 74.9 (7.1) years. Rhythm regularity could be assessed in 98.7% of ECGs recorded. 92 patients (5.1%) were found to have AF. Median [range]CHA_2DS_2-VASc score was 4 ([2–7) and median [range] HAS-BLED score was 2 (1–5).
Conclusion: handheld ECG recording can be used to identify AF in the primary care setting, with minimal training. The yield was relatively high.

1. Introduction

Atrial fibrillation is a major risk factor for stroke. Left atrial appendage thrombus formation occurs because of atrial stasis and because of changes in atrial wall composition [1]. Platelet activity increases and the coagulation cascades are activated when atrial fibrillation occurs. Stroke risk is especially prevalent in patients with heart failure, diabetes, hypertension, and vascular disease. This risk increases with age, and females are more likely to suffer stroke than males after adjustment for other risk factors. Stroke risk is modifiable through the use of anticoagulant drugs. Warfarin substantially reduces stroke risk in atrial fibrillation [2]. Direct oral anticoagulant (DOAC) drugs are at least as effective as warfarin and are supplanting the use of warfarin for this indication [3–6]

In the elderly population, atrial fibrillation is often asymptomatic or produces mild symptoms which do not prompt self-referral. Individuals with atrial fibrillation who are asymptomatic when they presented have a threefold higher incidence of prior stroke than do those who present with symptomatic atrial fibrillation [7]. This age group is at especially high risk of stroke when atrial fibrillation occurs, and many patients are likely to benefit from anticoagulants. In one study of asymptomatic, untreated individuals with atrial fibrillation, the stroke rate over 1.5 years follow-up was approximately 4% compared with 1% for an otherwise similar group who did not have atrial fibrillation. Undiagnosed atrial fibrillation is associated with high overall mortality rate compared with similar individuals without atrial fibrillation [8,9].

At present, atrial fibrillation is not identified in a systematic manner in primary care in Scotland. Pulse checking is a useful method of identifying atrial fibrillation but is not as reliable as the ECG [10]. The European Society of Cardiology currently recommends the use of an ECG rhythm strip to pulse palpation because of its limitations [11]. Within United Kingdom Quality and Outcomes Framework (QOF) standards, patients with chronic diseases e.g. cerebrovascular disease, diabetes, hypertension, vascular disease and chronic kidney disease (stage 3 and above) have been seen annually in primary care. These patients form an ideal potential target population for atrial fibrillation

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https://doi.org/10.1016/j.ijcard.2019.03.062
0167-5273/

screening. Opportunistic screening may be more efficient if individuals aged >65 years are targeted when they have other risk factors for stroke, or if and older age threshold (e.g. 70 years) is selected [12].

New technologies allow for easier identification of patients with atrial fibrillation. The 12 lead electrocardiogram is the gold standard for confirming this diagnosis, but for screening a simple single lead electrocardiogram can be used to identify P-waves and to assess the regularity of the rhythm. Recently, an adapter unit has been developed for smartphones and handheld computing devices (AliveCor®) which allows recording of such ECG waveforms [13]. These devices are primarily used as event recorders for patients with palpitation, but can also be used to record ECG data for screening for silent arrhythmias.

To maximise yield among individuals with moderate to high annual stroke risk, it makes sense to screen among older patients and/or those with other risk factors for stroke. Single timepoint screening of individuals over 65 years of age in the general population identifies (mostly persistent) atrial fibrillation in 1.4% of cases [14]. The European Society of Cardiology recommend opportunistic screening of all such individuals when medical contact is made [11]. When individuals over 75 years of age are screened with repeat recordings, a 3% yield is seen and this increases if individuals with known cardiovascular risk factors are selected [15–17].

This manuscript describes initial clinical experience in the implementation of an atrial fibrillation case-finding strategy among 22 primary care (general) practices across Scotland. This work was commissioned by the (Scottish) National Advisory committee for Stroke and the National Advisory Committee for Heart Disease, and was supported by the Digital Health Institute.

The objectives of this pilot clinical service were (i) to determine within the United Kingdom healthcare setting, the feasibility of screening for atrial fibrillation in primary care using a single lead ECG monitor, among individuals aged 65 years or older who have one or more cardiovascular risk factors; (ii) to estimate the yield of new atrial fibrillation cases, and the proportion of those patients who would be suitable for oral anticoagulation using standard risk scoring systems and bleeding risk systems.

2. Methods

(i) Selection of practices

A handheld ECG monitor unit was placed in each of twenty-three primary care practices in Scotland (three additional practices were included later on, because of poor recruitment from some practices). Practices were selected by lead cardiologists based in SE Scotland, West of Scotland, Tayside, Grampian and Fife. Each primary care practice had a designated member of staff responsible for ECG monitoring in that practice; in two cases this was a general practitioner and in all other cases this was a practice nurse. A single training session was provided by the study co-ordinator for each practice, in which single lead ECG recording technique was taught to maximise ECG recording quality. A weekly upload of ECG recordings was set up from each practice to the lead cardiologist. This manuscript describes the outcome of implementation of a clinical service and not a clinical research study. However, informed consent was obtained from patients and the implementation protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

(ii) Inclusion criteria

Patients aged 65 years or greater, attending their primary care practice for annual chronic disease assessment, were eligible for screening. Patients also had to have one or more of the following stroke risk factors: heart failure, hypertension, diabetes mellitus, previous stroke or transient ischaemic attack, peripheral or carotid arterial disease.

(iii) Exclusion criteria

Patients with a prior documented history of any atrial fibrillation episode were excluded.

(iv) ECG recording

30 second ECG recordings were made on patients with at least one risk factor in addition to age from the CHA_2DS_2-VASc scoring system. Patients with a prior history of AF were not included. These were patients attending for annual visits under the QOF chronic diseases recommendations. ECGs were recorded using an AliveCor® recorder attached to an Apple® iPod Touch® 5 handheld device. ECGs were recorded after hand washing, with hands rested on a table, away from mains equipment, to minimise noise. A unique number was assigned to each patient, and no patient-identifiable data were recorded on devices. ECG data and identifiers were uploaded onto the AliveCor (Kardia) server after each session. Anonymised ECG recordings were then available for analysis by the lead cardiologist for each region. In this pilot we did not utilise an automated ECG interpretation algorithm.

(v) Confirmation of diagnosis of atrial fibrillation

The lead cardiologist for each region received ECGs via the AliveCor (Kardia) server, using a secure protocol. The cardiologist adjudicated on whether or not the ECG was of interpretable quality, and if interpretable, whether atrial fibrillation was present or not.* Patients with a provisional diagnosis of atrial fibrillation based on the handheld ECG recording were referred for a 12 lead ECG as per local protocols. All ECGs were examined by a second cardiologist, and in cases in which there was disagreement about the presence or absence of atrial fibrillation, practices were asked to regard the patient as having suspected atrial fibrillation. As local practice varies between regions in Scotland, the screening protocol did not specify how patients were to be managed after AF detection, and general practitioners were recommended to follow their normal local practice for managing a patient with suspected AF.

(vi) Data collection

Additional medical history data were collected for all patients identified to have atrial fibrillation. These data were collected to enable the investigators to calculate stroke and bleeding risk using the following scoring systems [18–21]:

CHA_2DS_2-VAS_c – used to assess stroke risk in patients with nonvalvular atrial fibrillation.

HAS-BLED – accounts for some CHA_2DS_2-VAS_c risk factors, plus bleeding history, labile INR, abnormal liver and renal function, and current hypertension in estimating bleeding risk from oral anticoagulation.

Anticoagulant and antiplatelet drug history were also collected.

2.1. Outcome measures

The main outcome measure was:

- prevalence of atrial fibrillation among individuals aged >65 years who have other risk factors for stroke (as encompassed in the CHA_2DS_2-VAS_c scoring system)

Secondary pre-defined outcome measures were:

- proportion of recorded ECGs of interpretable quality
- proportion of patients with atrial fibrillation who would be suitable for oral anticoagulation
- proportion of new patients with HAS-BLED score of 3 or more points who may be unsuitable for oral anticoagulation because of bleeding risk

(vii) Assessment of quality of handheld ECG recordings

The quality of unfiltered ECG recordings was graded by the local cardiologist against a set of predefined criteria as follows: grade 1: cannot be interpreted; grade 2: noisy baseline. P-waves may be unclear if present, but regularity of rhythm can be assessed; grade 3: moderate baseline interference or noise. P-waves clear if present; grade 4: minor interference or noise; grade 5: no noise, very clear ECG.

2.2. Statistical analysis

Descriptive statistics are used to present CHA_2DS_2-VASc and HAS-BLED scores for the patients identified with atrial fibrillation. As distributions were likely to be positively skewed we present data as median (range).

3. Results

3.1. Data acquisition

Practice training visits took place between June and July 2014. The screening pilot commenced in August 2014 and was completed in October 2015. 2124 patients were identified for screening. Single lead ECGs were recorded and analysed in 1805 patients (703 female and 1102 male), mean (SD) age 74.9 (7.1) years. All patients were confirmed to have at least one risk factor in addition to age from the CHA_2DS_2-VASc scoring system.

In 319 cases ECG data were missing because of incorrect entry of study data onto the recorder, or because of accidental deletion of ECGs before uploading. Most of the data loss occurred in the first two months of the study.

Of the 1805 patients, 92 (5.1%) were identified to have atrial fibrillation. 175 patients (9.7%) had at least two (atrial or ventricular) ectopic beats during the 30 s recording.

Among the patients confirmed to have atrial fibrillation, the breakdown of CHA_2DS_2-VAS_c scores is summarised in Table 1. The breakdown of HAS-BLED scores is summarised in Table 2.

3.2. Qualitative assessment of handheld ECG recordings

Rhythm regularity could be assessed in 1780 (98.7%) cases. In 427 (23.7%) the ECG quality was excellent. Overall, mean (SD) ECG quality was 3.67 (1.01). There was little variation between regions in ECG quality, with mean (SD) values for each region as follows: Fife 3.84 (0.94), Lothian 3.68 (1.03), West of Scotland 3.61 (1.01), Grampian 3.67 (1.05), Tayside 3.51 (1.04). P-waves could be seen among patients identified not to have atrial fibrillation in 94% of cases.

3.3. Stroke risk

Future annual stroke risk was estimated using the CHA_2DS_2-VAS_C score. Median [range]CHA_2DS_2-VASc score was 4 (2–7). The distribution of CHA_2DS_2-VAS_C scores is shown in Fig. 1.

No patients had CHA_2DS_2-VAS_C score of 0 or 1 point because the predefined screening criteria stipulated that patients should be age 65 years or greater and have one other CHA_2DS_2-VAS_C component risk factor. Median (range) CHA_2DS_2-VAS_C score of those with AF was 4 (2–7) and of those without AF was 4 (2–7). Each patient was assigned an annual bleeding risk based on data from the original validation study for CHA_2DS_2-VAS_C. Median estimated annual stroke risk for patients identified to have atrial fibrillation was 4 (2.2–9.8) percent. The distribution of individual stroke risk factors within the CHA_2DS_2-VAS_C score are shown in Table 1. Excluding age, which was an inclusion criterion for screening, hypertension and vascular disease were the most prevalent risk factors.

3.4. Bleeding risk

Future bleeding risk was estimated using the HAS-BLED score. Median [range] HAS-BLED score was 2 (1–5). The distribution of HAS-BLED scores is shown in Fig. 2.

Median HAS-BLED score was 2 (1–5). Each patient was assigned an annual bleeding risk based on data from the Euro Heart Survey from which the HAS-BLED score was derivedPisters 2010. Median estimated annual stroke risk for patients identified to have atrial fibrillation was 1.8 (1.02–12.5) percent. The prevalence of bleeding risk factors within the HAS-BLED score are shown in Table 2. Excluding age, which was an inclusion criterion for screening, hepatic or renal dysfunction and previous stroke were the most prevalent risk factors.

3.5. Stroke risk among patients with high estimated bleeding risk

19 patients (22%) of patients identified with new atrial fibrillation had HAS-BLED score of three points or greater. Patients with HAS-BLED score at this level are considered at increased risk of major bleeding with warfarin (>5 major bleeding events per 100 patient years) [21]. The median CHA_2DS_2-VAS_C score of patients who had increased bleeding risk was 5 (4–7), identifying a group of patients in whom anticoagulation is likely still to be considered despite increased bleeding risk. The median (range) HAS-BLED score of patients with CHA_2DS_2-VASc score 1–3 points was 1 (1–2); with CHA_2DS_2-VASc score 4–5 points was 2 (1–4) and with CHA_2DS_2-VASc score 6–7 points was 3 (1–5).

Table 1
CHA_2DS_2-VAS_c scores of patients identified to have atrial fibrillation from handheld ECG recording.

Risk factor	Number	Percentage
Congestive heart failure	15	17.0
Hypertension	65	73.8
Age 65–74 years	36	40.9
Age > 74 years	52	59.1
Diabetes mellitus	26	29.5
Stroke or TIA	14	15.9
Vascular disease	32	36.6
Female gender	33	37.5

Table 2
HAS-BLED scores of patients identified to have atrial fibrillation from handheld ECG recording.

RISK FACTOR	Number of patients	Percentage
Current systolic BP > 160 mmHg	8	9.1
Liver/renal dysfunction	21	23.8
Previous stroke	14	15.9
Bleeding tendency	2	2.3
Labile INR	0	0
Age 65 years or greater	88	100
Drugs (NSAID/antiplatelet)	41	46.5
Alcohol misuse	0	0

3.6. Oral anticoagulant prescription

Of the 92 patients identified to have AF, 74 (80%) were prescribed an oral anticoagulant after diagnosis. Ten patients were not recommended anticoagulation because of perceived high bleeding risk and six declined anticoagulation.

4. Discussion

This pilot has examined the feasibility of implementing a screening programme for atrial fibrillation using a handheld, smartphone-based ECG recorder, among individuals aged >65 years who have risk factors for stroke. Once initial training and technical obstacles are overcome, it is feasible to use this technology to identify patients with previously undiagnosed atrial fibrillation in the community.

ECG quality was acceptable for identifying atrial fibrillation in most cases, but might be improved with refresher training sessions. In 98.7% of cases the ECG was of sufficient quality to identify an irregular rhythm. In 12.9% of cases the ECG quality was graded '2' and therefore not optimal. With the introduction of an automated algorithm to check ECG quality and identify atrial fibrillation, repeat ECG recording would be prompted to the user. Such algorithms are associated with sensitivity up to 99% and specificity up to 97% [22,23,24].

The yield for previously unidentified atrial fibrillation was 5%. While considerably greater than that seen in other population studies, such a high yield may partly be explained by the inclusion of a relatively high percentage of patients with risk factors such as diabetes or hypertension. In one study the prevalence of ECG observable atrial fibrillation in hypertensive patients of age 65 or greater was 6.7% [25]. In Engdahl's study of patients aged 75–76 years using the Zenicor device, AF was detected in >7% in patients who had one or more non age CHA_2DS_2-VASc risk factor. In these studies the high rate of detection of AF may be partly due to additional comorbidities and due to the methods of screening in which ECGs were recorded at multiple time points with a significantly higher detection rate than a single ECG [15,16,25]. The prevalence of AF in our cohort is considerably higher than that found in the SAFE study, but that study did not require pre-existing risk factors such as hypertension, diabetes or heart failure which would tend to increase the prevalence of AF [26]. The prevalence is also higher than that cited by Lowres et al. in a systematic review of 30 studies using a variety of detection methods [14]. Again these studies did not necessarily prespecify pre-existing stroke risk factors, and detection methods such as pulse palpation may produce a lower yield. Even accounting for this,

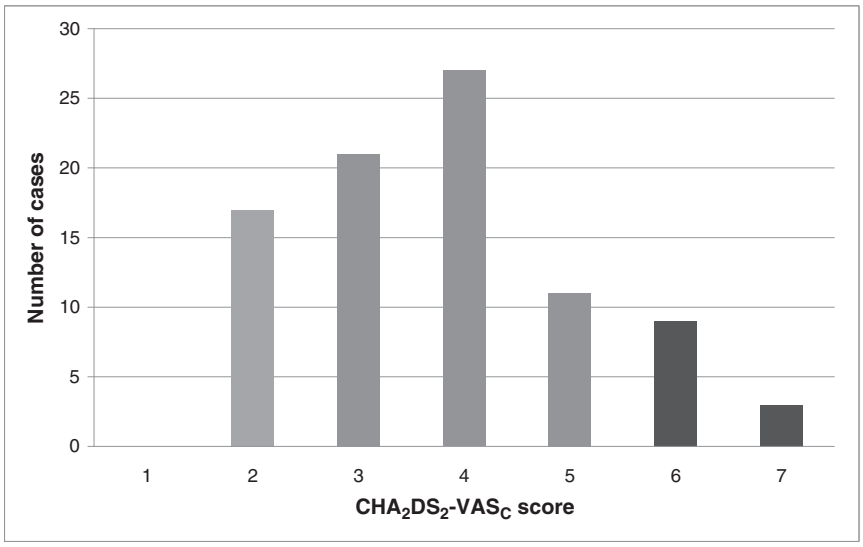

Fig. 1. Distribution of CHA_2DS_2-VAS_C scores among patients with newly identified atrial fibrillation.

the high prevalence of AF found in our cohort suggests under-detection of AF in primary care in Scotland. The yield for multiple ectopic beats was nearly 10%, and this indicates that methods which rely on identifying pulse irregularity alone (such as pulse checks, or blood pressure monitors with irregularity detection) may be prone to false positive error in this population. Among patients with atrial fibrillation the median CHA_2DS_2-VAS_C score was 4 points and median predicted annual stroke risk was 4%.

The University of Aberdeen Department of Health Economics are analysing the data from this pilot in detail, to make an estimate of the cost per case of atrial fibrillation identified, cost per stroke prevented, and the estimated additional burden from bleeding if patients are treated with anticoagulants. Below is a basic interpretation of the data which is preliminary only:

For every 1000 patients screened, 50 patients will be identified with previously unknown atrial fibrillation. With a predicted median annual stroke risk of 4%, this would mean that 2.4 strokes would occur every year if these patients went untreated (this figure accounts for the fact that stroke risk increases steeply when the CHA_2DS_2-VAS_C score is greater than the median). Anticoagulation with warfarin is known to reduce stroke risk by 64% relative to placebo treated patients, so warfarin would potentially prevent 1.5 strokes per year of treatment [2]. The use of the novel oral anticoagulants (NOACs) dabigatran or apixaban is associated with approximately 20% further stroke risk reduction over warfarin [3,4]. Thus, treatment of all patients identified with atrial fibrillation from a screening cohort of 1000 could prevent 1.7–1.8 strokes per year, or potentially up to 17–18 strokes over ten years of treatment.

Expected bleeding risk with oral anticoagulants also needs to be taken into account; this is defined as bleeding requiring transfusion of two or more units of packed red cells (or a fall in haemoglobin level of at least 2 g per decilitre), or intracranial bleeding. With NOACs the expected major bleeding risk would be 2.1% per year, or 21 major bleeding events over ten years requiring transfusion. The most important endpoint is intracranial bleeding, and based on data from the ARISTOTLE trial with apixaban, and RELY trial with dabigatran, expected risk would be 0.24% per year of treatment, or up to 2.4 intracranial bleeding events over 10 years [3,5].

Future studies need to examine the relationship between atrial fibrillation burden and stroke risk as for patients who have low burden intermittent rather than persistent atrial fibrillation, the risk- benefit balance of anticoagulation is less clear [28]. Studies of atrial fibrillation burden and stroke risk, using 'atrial high rate episodes' detected from implantable devices, suggest that any episodes of five minutes or greater is associated with increased risk of death or stroke [28]. The

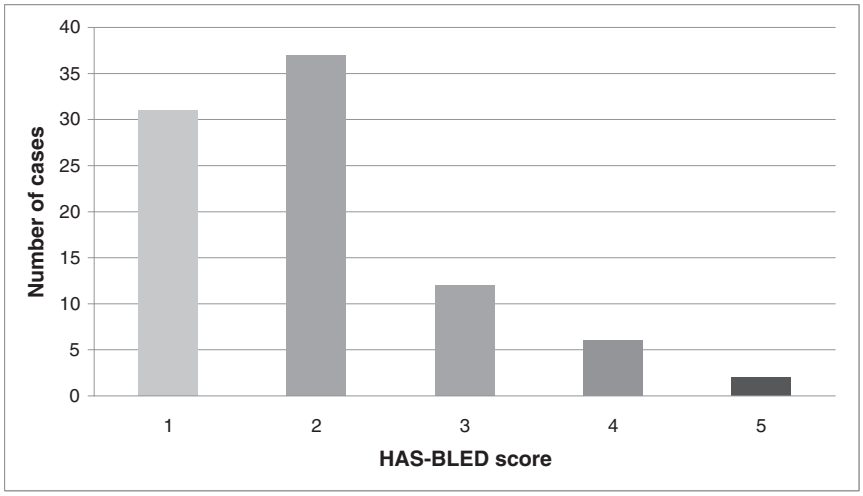

Fig. 2. Distribution of HAS-BLED scores among patients with newly identified atrial fibrillation.

temporal relationship between high rate episodes and stroke events is not direct [29]. Thus future case finding initiatives which focus on paroxysmal rather than persistent atrial fibrillation need to account for the complex and nonlinear relationship between AF burden and stroke risk.

Implementation of screening technologies has been explored by the Scottish Government Cross Party Working group on Atrial Fibrillation [30,31]. Implementation of technology to provide a clinical case finding service requires several steps. Firstly, it is best integrated into a primary care system in which patients with the cardiovascular risk factors encompassed by CHA_2DS_2-VASc are seen at least annually, as is the case in the United Kingdom. This has historically been done via the Quality and Outcomes Framework, which until 2017 provided an incentive mechanism for all primary care practices to offer review to all patients over 65 years of age annually and to assess chronic disease prevalence [32]. In Scotland 95% of practices participated fully in 2016–2017. In the future a similar or improved system needs to be put in place for identification and recall of these patients. This clinical pilot has identified the prevalence of undetected atrial fibrillation in a population not subject to systematic case finding, so the prevalence figure is known whereas the annual incidence is not. The frequency of screening will affect cost-effectiveness but annual screening may be tested in the first instance. Single session training of primary care nurses appears to produce acceptable ECG quality over the first year but refresher training may be required to maintain quality. ECG recording and stroke and bleeding score risk calculation will require approximately ten minutes of nurse time per patient. The use of high sensitivity and specificity automated ECG analysis will eliminate consultant costs for most single lead ECG screening. Once AF has been identified rapid referral for 12 lead ECG confirmation of atrial fibrillation is needed, and infrastructure put in place for ongoing investigation and management of those patients, for example through arrhythmia nurse specialist-led atrial fibrillation clinics with access to echocardiography and cardiologist review. Cardiologist recommendations at the time of diagnosis confirmation may help optimise the rate of anticoagulant use.

5. Conclusion

Screening for AF in primary care in the Scottish population, using handheld ECG monitors, is feasible and a clinically important yield is likely to result. It is possible that AF is underdiagnosed in this population compared with others studied. Upscaling will require significant infrastructure and resource planning.

5.1. Study limitations

The diagnostic accuracy of the device used could not be assessed in this study but has been well described by other investigators [22–24]. AF detection was carried out on on-consecutive patients in a clinical setting in which no additional staffing or infrastructure could be provided. The investigators relied on the ability of practice nurses to identify and record ECGs on patients when clinical time permitted. It is possible that selection bias occurred. The unusually high yield of AF found in this population would need to be confirmed in a subsequent analysis of yield as the clinical service is developed.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Acknowledgement

This work was funded by the Scottish Government via the National Advisory Committee for Stroke and the National Advisory Committee for Heart Disease. There was no grant ID associated with this funding.

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