






## ORIGINAL RESEARCH

# Atrial Fibrillation Screen, Management, and Guideline-Recommended Therapy in the Rural Primary Care Setting: A Cross-Sectional Study and Cost-Effectiveness Analysis of eHealth Tools to Support All Stages of Screening

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**BACKGROUND:** Internationally, most atrial fibrillation (AF) management guidelines recommend opportunistic screening for AF in people  $\geq 65$  years of age and oral anticoagulant treatment for those at high stroke risk ( $\text{CHA}_2\text{DS}_2\text{-VA} \geq 2$ ). However, gaps remain in screening and treatment.

**METHODS AND RESULTS:** General practitioners/nurses at practices in rural Australia ( $n=8$ ) screened eligible patients ( $\geq 65$  years of age without AF) using a smartphone ECG during practice visits. eHealth tools included electronic prompts, guideline-based electronic decision support, and regular data reports. Clinical audit tools extracted de-identified data. Results were compared with an earlier study in metropolitan practices ( $n=8$ ) and nonrandomized control practices ( $n=69$ ). Cost-effectiveness analysis compared population-based screening with no screening and included screening, treatment, and hospitalization costs for stroke and serious bleeding events. Patients ( $n=3103$ , 34%) were screened (mean age,  $75.1 \pm 6.8$  years; 47% men) and 36 (1.2%) new AF cases were confirmed (mean age, 77.0 years; 64% men; mean  $\text{CHA}_2\text{DS}_2\text{-VA}$ , 3.2). Oral anticoagulant treatment rates for patients with  $\text{CHA}_2\text{DS}_2\text{-VA} \geq 2$  were 82% (screen detected) versus 74% (preexisting AF) ( $P=NS$ ), similar to metropolitan and nonrandomized control practices. The incremental cost-effectiveness ratio for population-based screening was AU\$16 578 per quality-adjusted life year gained and AU\$84 383 per stroke prevented compared with no screening. National implementation would prevent 147 strokes per year. Increasing the proportion screened to 75% would prevent 177 additional strokes per year.

**CONCLUSIONS:** An AF screening program in rural practices, supported by eHealth tools, screened 34% of eligible patients and was cost-effective. Oral anticoagulant treatment rates were relatively high at baseline, trending upward during the study. Increasing the proportion screened would prevent many more strokes with minimal incremental cost-effectiveness ratio change. eHealth tools, including data reports, may be a valuable addition to future programs.

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**Key Words:** cost-effectiveness ■ digital health ■ general practice ■ primary care ■ rural ■ stroke prevention

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## CLINICAL PERSPECTIVE

### What Is New?

- This study extends the evidence base in rural areas by demonstrating that a screening program using eHealth tools in a rural general practice setting can successfully screen 34% of eligible patients with atrial fibrillation with guideline-indicated treatment rates >80% for screen-detected atrial fibrillation cases.
- Economic modeling showed that the program was cost-effective compared with no screening.
- Oral anticoagulant treatment rates for eligible patients were higher than previous studies at baseline (>70%) and were trending upward during the study (around 80%).

### What Are the Clinical Implications?

- eHealth tools, particularly customized data reports as part of an audit and feedback system, may be a valuable addition to screening programs.
- Half of the practices screened 40% to 50% of eligible patients, suggesting that this may represent a ceiling of patients captured by opportunistic atrial fibrillation screening programs in the general practice setting.
- Increasing the proportion screened would prevent many more strokes with minimal change to the incremental cost-effectiveness ratio.

## Nonstandard Abbreviations and Acronyms

<b>AF</b>	atrial fibrillation
<b>EDS</b>	electronic decision support
<b>GP</b>	general practitioner
<b>iECG</b>	handheld single-lead smartphone ECG
<b>ICER</b>	incremental cost-effectiveness ratio
<b>NOAC</b>	non-vitamin K dependent oral anticoagulant
<b>OAC</b>	oral anticoagulant
<b>QALY</b>	quality-adjusted life year
<b>QI</b>	quality improvement

Internationally, opportunistic screening for atrial fibrillation (AF) in people  $\geq 65$  years of age is now recommended by most guidelines.<sup>1,2</sup> Single timepoint screening detects undiagnosed AF, which is often asymptomatic, in approximately 1.4% of people in this age group.<sup>3</sup> Guidelines generally recommend treatment with oral anticoagulants (OACs),<sup>1,2</sup> which can reduce the risk of AF-related stroke by 64% for those at high risk (“sexless” CHA<sub>2</sub>DS<sub>2</sub>-VA [C = congestive heart

failure/left ventricular dysfunction, H = high blood pressure, A<sub>2</sub> = 75 years of age and older, D = diabetes mellitus, S<sub>2</sub> = stroke/transient ischemic attack/thromboembolism, V = vascular disease (coronary artery disease, myocardial infarction, peripheral artery disease, aortic plaque), A = 65–74 years of age] risk score  $\geq 2$ ).<sup>4</sup>

Large gaps in screening and treatment exist in practice. A survey conducted by *The Economist* in 2017 reported that only 11% of people  $\geq 65$  years of age were screened in Australian general practices in the previous fortnight.<sup>5</sup> Our previous 2018 study using eHealth tools conducted in metropolitan general practices increased screening to 16% of eligible patients.<sup>6</sup> In terms of treatment, rates have historically been 50% to 60%. However, since non-vitamin K dependent OAC (NOAC) medicines were introduced, an increase in treatment rates has been reported in Europe (>77% in England<sup>7</sup> and >65% in Denmark<sup>8</sup>). This trend was also reflected in our 2018 metropolitan study, which reported a treatment rate of 71% for those diagnosed with AF before the study, increasing to >80% for those diagnosed during the study period.<sup>6</sup>

Australians living in rural areas have more limited access to health services and worse cardiovascular outcomes.<sup>9</sup> The ratios of general practitioners (GPs), specialists, and nurses per capita of population are significantly lower in rural areas than in metropolitan areas, and access to specialist cardiac care is more limited.<sup>10,11</sup> Approximately 25% of the rural population suffers from cardiovascular diseases compared with 20% in metropolitan areas, and the likelihood of hospitalization and death resulting from cardiac events increases with the distance from metropolitan areas.<sup>12</sup> General practices play a key role in supporting cardiac health in rural areas as they tend to provide a broader range of community services compared with metropolitan practices.<sup>13</sup>

Several of our previous studies showed that opportunistic screening in primary care by GPs and nurses was feasible.<sup>6,14,15</sup> A suite of customized eHealth tools, including an automated prompt and electronic decision support (EDS), were found to be promising.<sup>6</sup> These tools have been refined and enhanced with a quality improvement (QI) focus<sup>16,17</sup> and are designed to support all stages of screening.

This study aims to improve the proportion of patients screened and treated for AF using the refined eHealth tools and to inform strategies on AF screening implementation in the rural setting. In addition, this study provides the first cost-effectiveness analysis in Australian general practice.

## METHODS

This study was conducted in a convenience sample of 8 rural general practices from September 2018 to July

2019 in rural New South Wales, Australia. Practices were required to be located outside a major city (generally categorized under the Australian Statistical Geography Standard–Remoteness Area 2016<sup>18</sup> code 2 “inner regional Australia”) and were recruited by advertisements in primary health network newsletters and by word of mouth. Participating practices provided written informed consent, and patients provided oral consent for screening. This study was approved by the University of Sydney Human Research Ethics Committee (Project No. 2017/1017; Clinical Trial Registration No. ACTRN1261800004268). The data and materials will not be made available to other researchers as data sharing is not permitted by our ethics committee approval. Researchers interested in the data, methods, or analysis can contact the corresponding author for more information.

The methods for this study have been previously described in detail.<sup>17</sup> Briefly, GPs and/or practice nurses offered screening for AF with smartphone handheld single-lead ECGs (iECGs) (KardiaMobile) to eligible patients attending the practice for any reason. Eligible patients were those ≥65 years of age without an existing AF diagnosis who had not already been screened with the iECG within the past 12 months. All follow-up for those with abnormal screening results according to the iECG app (“possible AF” or “unclassified”) and treatment decisions were at the discretion of the GP.

To support screening, practices were provided with eHealth tools (Figure 1).

- Screening prompt: An app located in a third-party hosting platform automatically extracted information from patients’ electronic medical records. Using this information in real time, a prompt appeared when an eligible patient’s file was opened. The iECG automated screening result was also recorded in this app.

- EDS: For those diagnosed with AF (either by screening or otherwise), the EDS app (also located on the third-party hosting platform) calculated their CHA<sub>2</sub>DS<sub>2</sub>-VA stroke risk score and made guideline recommendations regarding treatment. This app was part of the HealthTracker suite of cardiovascular QI tools.
- Tailored clinical audit data for QI reporting: Customized, de-identified clinical audit data extracts were obtained monthly from participating practices. These data were used to report back to practices and included data on the number and proportion screened, the number of patients with new AF, and the proportion treated according to guidelines.

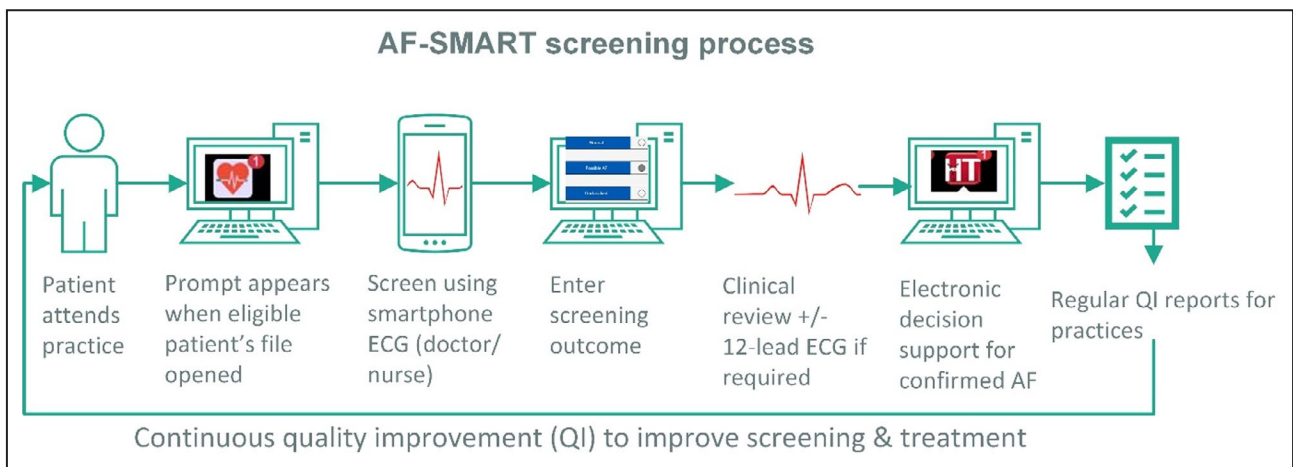
**Reimbursement**

Practices were paid \$1000 to cover study setup time and data extraction costs plus \$10 per patient screened (paid per 100 patients to encourage greater numbers). This was intended to cover the costs of screening in the Australian fee-for-service context and to replicate a real-world fee if screening was covered by Medicare. Screening was free for patients, although any usual consultation fees applied.

**Data Collection and Analysis**

De-identified data extracts included demographic, iECG screening, medication, and diagnostic information from the practices’ electronic patient records. The data extracts were designed to collect data for all active patients of the practices, that is, patients who had attended at least 3 times in the past 2 years and once in the past 6 months.

To provide additional context about broader screening and treatment trends, data from this study were compared with 2 other de-identified data sets:



**Figure 1. Screening process and eHealth tools adapted from our 2018 metropolitan study.<sup>6</sup>** AF indicates atrial fibrillation; QI, quality improvement.

the metropolitan group and the nonrandomized control group. These comparator data sets were collected from other Australian studies also using the HealthTracker app, with prospectively collected data using the same data extraction tool and data fields. The metropolitan group was from our 2018 AF screening study,<sup>6</sup> which included 8 metropolitan general practices. The nonrandomized control group was composed of 69 practices (64 metropolitan and 5 rural) that were using HealthTracker for general cardiovascular QI studies that did not involve AF screening. For the purposes of comparisons of treatment rates before and during the study period, the nonrandomized control group data were split into AF diagnoses before January 1, 2018 (baseline treatment rate) and AF diagnosed on or later than January 1, 2018 (AF diagnosed during the study period).

Descriptive analyses for the rural practices were carried out using Microsoft Excel. Descriptive analyses of nonrandomized control data were performed using R Statistical Programming, version 3.6.1.<sup>19</sup> Comparisons of treatment rates between groups were calculated using the Fisher exact test (2-sided *P* values) performed using 2×2 contingency tables (GraphPad Prism version 7.04) with significance set a priori at *P*<0.05. Although our protocol paper specified a chi-square test, the Fisher exact test was used as it was more accurate with the small numbers involved.

A detailed process evaluation was carried out using mixed methods, including semistructured interviews with selected practice staff. This evaluation examined outcomes related to implementation success and the acceptability/competing demands of the screening program. Methods and results of this evaluation have been described elsewhere.<sup>16</sup>

### Cost-Effectiveness Analysis

The iECG screening program was evaluated by comparing population-based AF screening with no screening from an Australian health funder perspective. The economic model developed in the SEARCH-AF (Screening Education and Recognition in Community Pharmacies of Atrial Fibrillation)<sup>20</sup> pharmacy screening study was adapted to evaluate iECG screening in general practice. The model has previously been explained in detail.<sup>20</sup> Briefly, the model compares the cost of iECG screening, diagnosis, and treatment in general practice to diagnosed AF in the unscreened population of Australian men and women 65 to 84 years of age. That is, it compares population-based AF screening to no screening. It assumes a base rate of AF (both diagnosed and unknown) and follows a cohort of the population 65 to 84 years of age for 10 years with annual stroke events and all-cause mortality.

Stroke costs included hospitalization, rehabilitation, and other ongoing medical costs. For this study, the model was updated to include the cost of an echocardiogram for those diagnosed and the costs of major bleeding episodes for those on OAC treatment and a treatment regimen consistent with current trends (that is, including NOACs prescribed at rates observed in the current study).

The model included several key assumptions (full list included as Table S1).

- The proportion screened was that observed in this study.
- The prevalence of diagnosed AF in the population ≥65 years of age was 4.4%.<sup>3</sup>
- The prevalence of unknown AF in the population ≥65 years of age was 1.4%.<sup>3</sup>
- OAC and antiplatelet treatment rates were as observed for all patients diagnosed during the study period (both screen detected and otherwise detected).
- The iECG test sensitivity was 97%, and specificity was 92%.
- The cost per screen was \$20.
- For those diagnosed with AF, annual treatment and monitoring costs for those on OACs were \$1063.78 (warfarin) and \$1401.73 (mean cost for NOACs) and included annual costs of medication, pathology, GP, and specialist visits.

Costs for hospitalization for stroke were obtained from Cadilhac et al<sup>21</sup> and were updated to 2019 prices using the Australian Health Price Deflator Index. In addition, a present value of 5.09 quality-adjusted life years (QALYs) (gained over a lifetime) was used for each ischemic stroke prevented by screening.<sup>21</sup>

Results are presented in Australian dollars as an incremental cost-effectiveness ratio (ICER) per stroke avoided and per QALY gained for population-based screening compared with no screening. Sensitivity analyses were also performed for different proportions of patients screened, price reductions in NOAC medicines, differences in iECG test sensitivity and specificity, differences in OAC treatment rates, and differences in rates of major bleeding episodes.

### Outcomes

Key study outcomes were the following:<sup>17</sup>

- the proportion of screened patients with confirmed new AF,
- the proportion of AF and screened patients where the EDS was accessed,
- the proportion of patients with AF diagnosed during the study period in the OAC recommended category



(CHA<sub>2</sub>DS<sub>2</sub>-VA risk score $\geq$ 2)<sup>1</sup> who were prescribed an OAC according to guidelines,

- baseline AF prevalence in patients  $\geq$ 65 years of age compared with metropolitan and nonrandomized control groups,
- new screen-detected AF incidence at the end of the study period in patients  $\geq$ 65 years of age compared with the metropolitan and nonrandomized control groups, and
- rates of OAC and antiplatelet treatment at baseline and completion for patients in the OAC recommended category compared with the metropolitan and nonrandomized control groups.

## RESULTS

### Screening, Diagnosis, and Treatment

A total of 8 general practices were recruited and screened a total of 3103 eligible patients (mean age, 75.1 $\pm$ 6.8 years; 47% men) during the study period. The median screening period was 4.6 months (range, 1.7–7.5 months). Practices screened a mean of 34% (median 35%) of eligible patients (range, 9%–51% per practice), with 4 of 8 practices screening  $>$ 40% of eligible patients (Figure 2). In general, screening was highest in the first 1 to 2 months and declined thereafter. The mean proportion of all eligible patients who attended the practices during the study period was 94%. GPs (n=22) screened 31% (range, 1–182 per GP) of patients and nurses (n=40) screened 69% (range, 1–192 per nurse). According to the iECG automated algorithm (as entered into the app by GPs/nurses), 83% of screenings were normal, 13% were unclassified, and 4% were possible AF.

In total, 36 (1.2%) of new cases of screen-detected AF were confirmed (mean age, 77.0 years; 64% men; mean CHA<sub>2</sub>DS<sub>2</sub>-VA, 3.2) (Table 1). The proportion of screen-detected patients with AF with at least 1 non-age or sex risk factor was 83%, and the proportion in the OAC recommended category (CHA<sub>2</sub>DS<sub>2</sub>-VA $\geq$ 2) was 94%. Characteristics and CHA<sub>2</sub>DS<sub>2</sub>-VA groups for those with screen-detected AF, otherwise-detected AF (during the study period), and AF detected before the study are presented in Table 1.

OAC treatment rates of patients with AF with CHA<sub>2</sub>DS<sub>2</sub>-VA $\geq$ 2 were 82% (screen-detected), 75% (otherwise-detected during study period), and 74% (preexisting AF), with no significant differences between treatment rates in the screen-detected group and other groups (Table 1). The EDS was accessed for 54 of 1337 (4%) patients 65 years of age and older with AF and for 4 of 36 (11%) patients with new screen-detected AF.

### AF Prevalence and Treatment Rates Compared With Metropolitan and Nonrandomized Control Groups

The baseline prevalence of AF in the rural and metropolitan practices and nonrandomized control groups ranged from 9% to 12% (Table 2).

There were no significant differences between the rural and metropolitan practices' treatment rates of those with AF detected before the study or during the study (screen-detected and otherwise-detected) (Table 2). Likewise, the treatment rates in the rural practices were similar to those in the nonrandomized control practices at baseline and during the study period (Table 2). The OAC treatment rates in all 3 cohorts tended to increase from baseline (Table 2), in contrast to antiplatelets.

### Cost-Effectiveness Analysis

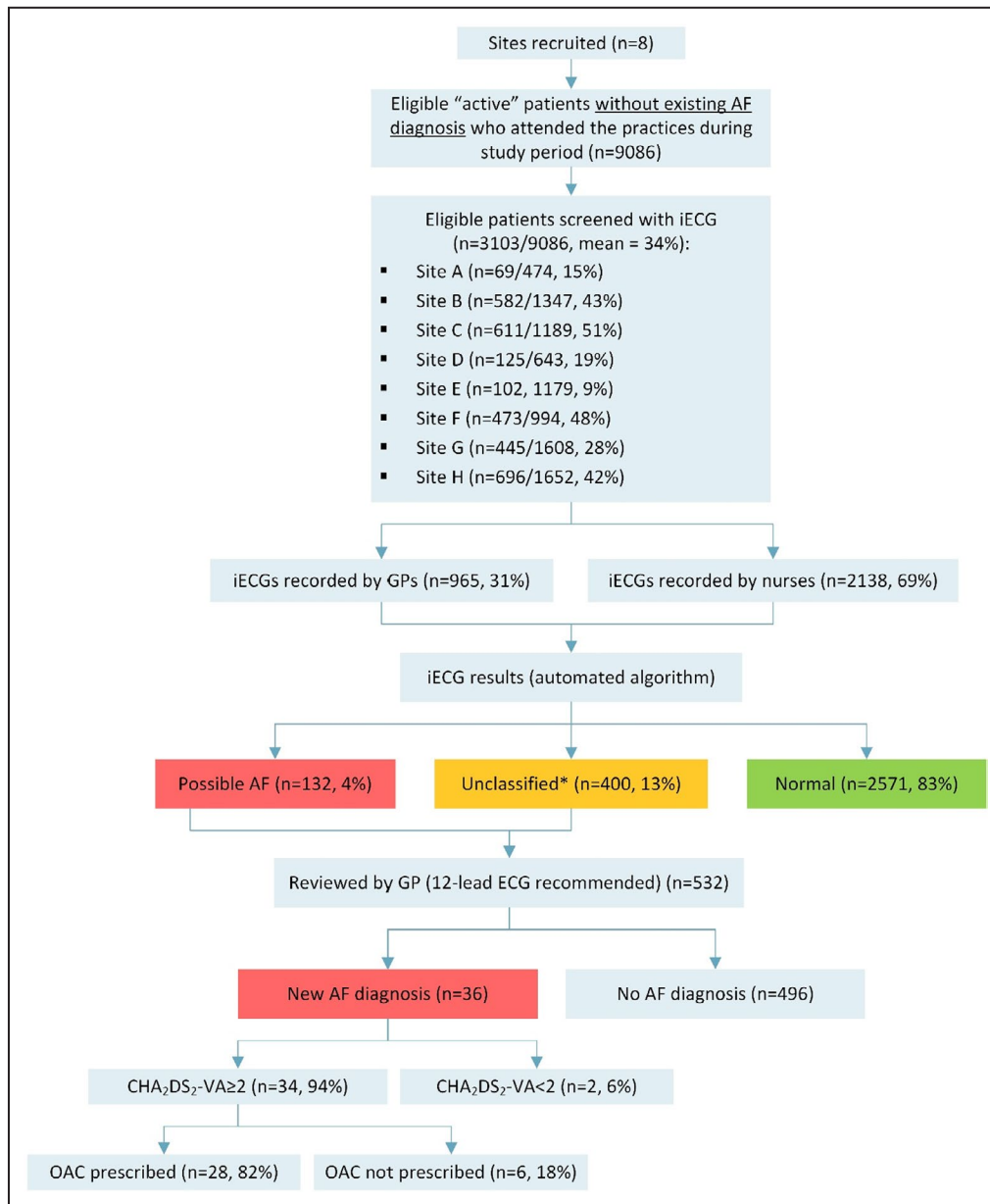
Our cost-effectiveness modeling showed that for population-based AF screening for Australian men and women 65 to 84 years of age, assuming a 34% screening participation rate with a treatment rate of 82% in the screened population and a test sensitivity of 97% and specificity of 92%, the ICER per QALY gained was AU\$16 578 and the ICER per stroke avoided was  $\geq$ 84 383 compared with no screening.

Increasing the screening participation rate has a negligible effect on the ICER, but substantially increases the number of strokes prevented, that is, effectiveness (Table 3). Increasing the screening participation rate from 34% to 50% raises the number of strokes prevented from the base case of 147 per year to 216 per year (or 1467 to 2157 over 10 years). With a 75% screening participation rate, a total of 324 strokes are prevented each year (or 3235 strokes over 10 years) when compared with the no screening scenario.

Raising the OAC treatment rate also prevents more strokes, with a relatively small impact on the ICER. An OAC treatment rate of 90% (in both the screened and unscreened populations) would prevent a total of 1610 strokes over 10 years, with an ICER per QALY gained of \$16 188 compared with no screening.

For population-based screening, lowering the cost of NOAC treatment decreases the ICER per QALY gained to AU\$14 997 (12.5% price reduction) or AU\$13 416 (25% price reduction) compared with no screening.

Furthermore, changes to the iECG test sensitivity and specificity did not have material impacts on the ICER per stroke prevented nor the ICER per QALY gained compared with no screening. However, increasing the test sensitivity to 100% did prevent an additional 45 strokes over 10 years. Similarly, sensitivity analyses



**Figure 2. Screening flowchart.**

\*Unclassified results may be attributed to sinus bradycardia, sinus tachycardia, left or right bundle branch block, multiple ectopic beats, or other arrhythmias. AF indicates atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-VA, C = congestive heart failure/left ventricular dysfunction, H = high blood pressure, A<sub>2</sub> = 75 years of age and older, D = diabetes mellitus, S<sub>2</sub> = stroke/transient ischemic attack/thromboembolism, V = vascular disease (coronary artery disease, myocardial infarction, peripheral artery disease, aortic plaque), A = 65 to 74 years of age; GP, general practitioner; iECG, handheld single-lead smartphone ECG; and OAC, oral anticoagulant.

regarding major bleeding rates did not have a material impact on the ICER per stroke prevented nor the ICER per QALY gained compared with no screening.

## DISCUSSION

This study investigated the impact of an AF screening program in rural general practices using an iECG together

with a suite of custom-designed eHealth tools designed to increase the proportion screened and treated for AF in accordance with guidelines. GPs and nurses at participating practices screened a total of 3103 eligible patients, and 36 (1.2%) new cases of AF were confirmed, with 82% prescribed OAC according to guidelines.

This study featured a unique suite of integrated, customized eHealth tools to support all stages of AF screening and treatment in general practice. These

**Table 1. Characteristics and Stroke Risk of Those ≥65 Years of Age With AF**

	Screen-Detected AF	Otherwise-Detected AF During Study Period	Baseline: AF Diagnosed Before Study
	(n=36)	(n=58)	(n=1243)
Age, y, mean±SD	77.0±6.1	77.0±8.4	79.2±7.8
Male, n (%)	23 (64)	32 (55)	662 (53)
Mean CHA <sub>2</sub> DS <sub>2</sub> -VA	3.2	3.3	3.7
CHA <sub>2</sub> DS <sub>2</sub> -VA≥2, n (% of total)	34 (94)	55 (95)	1223 (98)
CHA <sub>2</sub> DS <sub>2</sub> -VA≥2 and prescribed OACs, n (% of those with CHA <sub>2</sub> DS <sub>2</sub> -VA≥2)	28 (82)	41 (75) <i>P</i> =0.444*	908 (74) <i>P</i> =0.326*
≥1 nonage or sex risk factors, n (% of total)	30 (83)	54 (93)	1178 (95)

AF indicates atrial fibrillation; and CHA<sub>2</sub>DS<sub>2</sub>-VA, C = congestive heart failure/left ventricular dysfunction, H = high blood pressure, A<sub>2</sub> = 75 years of age and older, D = diabetes mellitus, S<sub>2</sub> = stroke/transient ischemic attack/thromboembolism, V = vascular disease (coronary artery disease, myocardial infarction, peripheral artery disease, aortic plaque), A = 65 to 74 years of age; and OAC, oral anticoagulant.

\**P* value for comparison to screen-detected AF.

tools were refined following our metropolitan study<sup>6</sup> and included an automated screening prompt (with improved visibility and reliability), an EDS app to guide treatment, and de-identified data extracts and with regular QI audit and feedback reporting to practices. We are not aware of any other studies that include tools to cover all stages of AF screening and treatment, including customized feedback. In particular, the refined screening prompt and the improved QI reporting were useful and motivating for participating GPs and nurses.<sup>16</sup>

### Proportion Screened and Treated

Practices screened 34% of eligible patients who attended during the study period, which is substantially higher than the 16% achieved in our metropolitan study.<sup>6</sup> Half of the study practices were able to screen >40% of eligible patients, although 51% was the maximum reached. It appeared that even practices with broad uptake and high motivation across staff were not able to capture more than 50% of eligible patients, which GPs and nurses indicated was largely attributed to time constraints and technical issues (eg, difficulty taking a

**Table 2. Treatment Rates and Comparisons Between Groups: Patients ≥65 Years of Age With AF**

	Rural Practices (n=8)	Metropolitan Practices (n=8)	Nonrandomized Control Practices (n=69)
Total active* patients ≥65 years of age	10 896	13 679	30 116
Baseline AF prevalence	12%	11%	9%
Baseline: AF detected before study with CHA <sub>2</sub> DS <sub>2</sub> -VA≥2			
Total, n	1223	1306	1875
Prescribed OAC, n (%)	908 (74)	933 (71) <i>P</i> =0.118†	1450 (77) <i>P</i> =0.052†
Prescribed antiplatelet alone, n (%)	178 (15)	213 (16)	248 (13)
Not prescribed OAC or antiplatelet, n (%)	137 (11)	160 (12)	177 (9)
Screen-detected AF during study period with CHA <sub>2</sub> DS <sub>2</sub> -VA≥2			
Total, n	34	18	N/A
Prescribed OAC, n (%)	28 (82)	15 (83) <i>P</i> >0.999†	N/A
Prescribed antiplatelet alone, n (%)	1 (3)	1 (6)	N/A
Not prescribed OAC or antiplatelet, n (%)	5 (15)	2 (11)	N/A
All AF detected during study period (screen detected+otherwise detected) with CHA <sub>2</sub> DS <sub>2</sub> -VA≥2			
Total, n	89	64	399
Prescribed OAC, n (%)	69 (78)	54 (84) <i>P</i> =0.312†	333 (83) <i>P</i> =0.218†
Prescribed antiplatelet alone, n (%)	7 (8)	3 (5)	29 (7)
Not prescribed OAC or antiplatelet, n (%)	13 (15)	7 (11)	37 (9)

AF indicates atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-VA, C = congestive heart failure/left ventricular dysfunction, H = high blood pressure, A<sub>2</sub> = 75 years of age and older, D = diabetes mellitus, S<sub>2</sub> = stroke/transient ischemic attack/thromboembolism, V = vascular disease (coronary artery disease, myocardial infarction, peripheral artery disease, aortic plaque), A = 65 to 74 years of age; and OAC, oral anticoagulant.

\*Active patients are those who attended the practice at least 3 times in the past 2 years and once in the past 6 months.

†*P* value for comparison to rural practices.

**Table 3. Cost-Effectiveness of Population-Based AF Screening Compared With No Screening and Sensitivity Analyses Over 10 Years**

	Base Case				
Screening participation rate, %	34	50	60	70	75
Number of strokes prevented	1467	2157	2588	3020	3235
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$83 304	\$82 922	\$82 649	\$82 540
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$16 366	\$16 291	\$16 238	\$16 216
NOAC price reduction	-	12.5%	25%		
Number of strokes prevented	1467	1467	1467		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$76 336	\$68 289		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$14 997	\$13 416		
iECG test sensitivity	97%	92%	100%		
Number of strokes prevented	1467	1391	1512		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$85 940	\$83 524		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$16 884	\$16 409		
iECG test specificity	92%	89%	93%		
Number of strokes prevented	1467	1467	1467		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$86 818	\$83 571		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$17 057	\$16 419		
OAC treatment rate	74%/82% <sup>†</sup>	55%	90%		
Number of strokes prevented	1467	984	1610		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$97 731	\$82 397		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$19 201	\$16 188		
Major bleeds—crude excess incidence rate per 1000 person-years of major bleeds for those 65–74 years of age	4.8	2.2	7.4		
Number of strokes prevented	1467	1467	1467		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$83 409	\$85 358		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$16 387	\$16 770		
Major bleeds—crude excess incidence rate per 1000 person-years of major bleeds for those 75–84 years of age	4.2	1.3	7.2		
Number of strokes prevented	1467	1467	1467		
Net cost [ICER] per stroke prevented compared with no screening	\$84 383	\$83 753	\$85 035		
Net cost [ICER] per QALY gained compared with no screening	\$16 578	\$16 454	\$16 706		

AF indicates atrial fibrillation; ICER, incremental cost effectiveness ratio; QALY, quality-adjusted life year; NOAC, non-vitamin K dependent anticoagulant; OAC, oral anticoagulant; and \$ = Australian dollars (AUD).

\*Unscreened population.

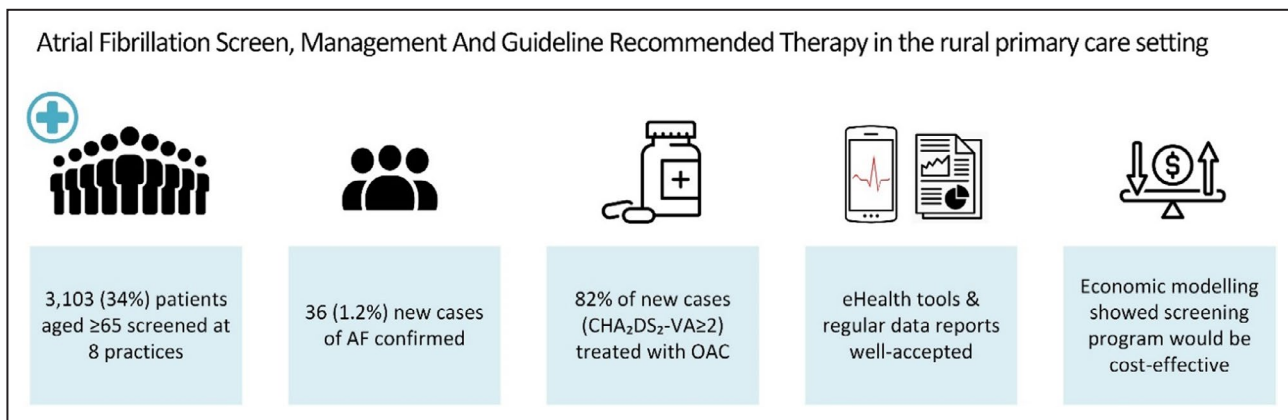
<sup>†</sup>Screened population.

reading on some patients).<sup>16</sup> Key features of the most successful practices included leadership from a senior GP “screening champion,” clear protocols for follow-up of abnormal results for nurse-led screening, and

sufficient staff time allocation for screening. These are discussed in detail in our qualitative realist evaluation.<sup>16</sup>

A recent study of AF screening in 184 Canadian practices was able to screen 42% of eligible





**Figure 3. Summary of findings.**

AF indicates atrial fibrillation; CHA<sub>2</sub>DS<sub>2</sub>-VA, C = congestive heart failure/left ventricular dysfunction, H = high blood pressure, A<sub>2</sub> = 75 years of age and older, D = diabetes mellitus, S<sub>2</sub> = stroke/transient ischemic attack/thromboembolism, V = vascular disease (coronary artery disease, myocardial infarction, peripheral artery disease, aortic plaque), A = 65 to 74 years of age; and OAC, oral anticoagulant.

patients.<sup>22</sup> In addition, a study from the Netherlands where patients  $\geq 65$  years of age were screened in 10 general practices during influenza vaccination sessions captured 35% of eligible patients, which is almost identical to our study.<sup>23</sup> These results suggest that 40% to 50% may be a “ceiling” of eligible patients captured by an opportunistic screening program in general practice.

As with the metropolitan study, treatment rates were high at baseline ( $>70\%$ ) compared with historical Australian data and increased during the study. The treatment rates were highest for screen-detected AF ( $>80\%$ ). These treatment rates and trends were similar to those in the nonrandomized control practices. These rates are higher than previously reported in Australia, which were about 55% to 60%<sup>24</sup> before the introduction of NOACs (preferred by the Australian guidelines).<sup>1</sup> Our results show a similar trend to recent European treatment rates of around 65% to 80%<sup>8,25,26</sup> since the introduction of NOACs.

Our results also show a decline in antiplatelet prescription for those not on OACs. Of the patients diagnosed during the study period ( $\geq 65$  years of age with CHA<sub>2</sub>DS<sub>2</sub>-VA $\geq 2$ ) who were not prescribed OACs ( $n=20$ ), only a minority were prescribed antiplatelets alone ( $n=7$ ) with the remainder on no therapy ( $n=13$ ). Of the 7 patients prescribed antiplatelets before being diagnosed with AF (1 of whom had cardiovascular disease) and another 3 of these patients also had cardiovascular disease, which may be the reason antiplatelets were prescribed. This suggests that the prescription of antiplatelets alone for AF may be declining, as was recently reported in a US study<sup>27</sup> and that effectively the prescribing decision is becoming “OAC or no treatment.”

## Rural Setting

This study extends the evidence base in rural areas and shows that a screening program in the rural general practice setting can successfully screen a large number of eligible patients with AF with guideline-indicated treatment rates  $>80\%$  for screen-detected AF cases. A screening program using pulse palpation in rural general practice in Ireland achieved a similar reach to our study (30% of the general practice population  $\geq 65$  years of age screened), although OAC treatment rates were lower (65%).<sup>28</sup> The authors noted important differences regarding the density of population in rural studies compared with metropolitan studies, with implications for rural patients’ access to primary and secondary care.

Prevention programs suitable for rural areas are particularly important given that people living in these areas tend to have worse cardiovascular outcomes and less access to specialist medical services.<sup>9</sup> Rural general practice is potentially an ideal setting for implementation of innovative primary care-based cardiac programs, such as ours, which contribute to upskilling GPs in cardiac care, training nurses to provide cardiac education/screening, and using novel technology.

## Cost-Effectiveness

Our cost-effectiveness modeling showed that for population-based AF screening in general practice for Australian men and women 65 to 84 years of age, the ICER per QALY gained was AU\$16 578 and the ICER per stroke avoided was AU\$84 383 compared with no screening. Increasing the proportion screened from 34% to 75% would prevent an additional 177 strokes per year (or 1768 strokes over 10 years) with a

negligible effect on the ICER. These figures are higher than for SEARCH-AF,<sup>20</sup> largely driven by an increased uptake of OAC treatment rates and in particular the higher prescription rates of NOACs. The increased proportion of people treated with OAC reduces the ICER, although this is offset by the higher cost of treatment with NOACs. These figures are well within the accepted thresholds of Australian government health expenditures.<sup>29</sup> This is consistent with several other studies, which found AF screening to be cost-effective<sup>30</sup> or even cost-saving.<sup>31</sup>

Importantly, although we were able to screen 34% of eligible people with these tools (and have suggested that 40%–50% may be a “ceiling” of patients captured with opportunistic screening programs), these analyses highlight the impact of increasing the proportion screened in terms of stroke prevention and the need to consider new approaches to break the 40% to 50% barrier.

## Limitations

The proportion of non-normal results according to the iECG device algorithm was relatively high at 17% (possible AF, 4%; unclassified, 13%). This added to the workload substantially for practices, as was also noted in a recent Canadian study,<sup>22</sup> as all of these patients require some degree of follow-up. In relation to the possible AF readings, it is likely that some were paroxysmal AF (AF not present on a subsequent 12-lead ECG) or false positives (eg, attributed to sinus arrhythmia, multiple atrial ectopics, or a poor quality trace). It is also possible that some AF diagnoses were not recorded in the clinical system (see Limitations below). In relation to the unclassified results, previous studies have usually reported lower rates closer to 10%.<sup>6,14</sup> Improvements in the device algorithm (eg to identify sinus tachycardia/bradycardia) and training staff in techniques to take clearer readings will reduce this burden. We note that the research team was not able to review the iECGs and relied on GPs/nurses to manually enter the device’s interpretation into the AF app. The iECG automated algorithm has been reported to have a sensitivity of 97% and specificity of 92%.<sup>20</sup>

The EDS was only used for a low proportion of patients. This is probably because it was in a separate app and was not accessed by GPs as it required extra clicks. Ideally, an EDS would need to be a more integral part of the electronic medical record system. Alternatively, an automatic calculation of patients’ CHA<sub>2</sub>DS<sub>2</sub>-VA scores in the electronic medical record would assist, particularly if it included an alert to review treatment when the score changed (especially when it exceeds a treatment-recommendation threshold).

The study relied on de-identified data collected from practices. This was routinely collected general practice data with all its inherent limitations. For example, if GPs recorded a diagnosis of AF in the free-text notes section instead of adding it as a condition from a drop-down list, this would not be caught in our data, meaning our figures may underestimate the true rate of AF detected during the study. In addition, these data were limited to active patients because of the definition in the data collection tool. “Active patients” were defined as those who had attended the practice at least 3 times in the past 2 years and once in the past 6 months. Therefore, our data may be biased toward people with more chronic conditions requiring more frequent attendance at the practice.

There were some limitations in relation to the cost-effectiveness analysis. A key methodological limitation is that a probabilistic sensitivity analysis was not undertaken to show model uncertainty, and therefore the model only reports point estimates on cost-effectiveness. However, this is consistent with the main purpose of the model, which was to provide an estimate of the cost-effectiveness and number of strokes prevented if the AF-SMART system was implemented nationally. In addition, the model has not been validated or calibrated to test whether predicted events are consistent with observed data.

## CONCLUSIONS

An AF screening program in rural general practices, supported by eHealth tools, screened 34% of eligible patients, with 82% of new screen-detected cases treated according to guideline (Figure 3). Half of the practices screened 40% to 50% of eligible patients, suggesting that this may represent a “ceiling” of patients captured by opportunistic AF screening programs. OAC treatment rates were higher than previous studies at baseline and were trending upward during the study. Increasing the proportion screened would prevent many more strokes with minimal changes to the ICER. This may require new methods to break through the ceiling captured by numerous opportunistic programs. eHealth tools, particularly customized data reports as part of an audit and feedback system, may be a valuable addition to future screening programs.

## ARTICLE INFORMATION

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### Supplementary Materials

#### Table S1

#### References 32–38

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# **SUPPLEMENTAL MATERIAL**



**Table S1. Cost-effectiveness model assumptions.**

Item	Cost/measure	Details	Source
Prevalence of known AF in the population aged 65-84 years	4.4%		Lowres et al, 2013 <sup>32</sup>
Prevalence of unknown AF in the population aged 65-84 years	1.4%		Lowres et al, 2019 <sup>3</sup>
iECG test sensitivity iECG test specificity	97% (95% CI: 92-100%) 92% (95% CI: 89-93%)		Lowres et al, 2014 <sup>20</sup>
Population	1,113,661(Male 65-74) 1,168,074(Female 65-74) 576,829 (Male 75-84) 658,438 (Female 75-84)	June 2019	Australian Bureau of Statistics, 2019 <sup>33</sup>
OAC treatment rates (unscreened population)	OAC: 74% Antiplatelet (alone) / no treatment: 26%		AF-SMART rural results section [baseline data]
OAC treatment rates (screened population)	OAC: 82% Antiplatelet (alone)/no treatment: 15%		AF-SMART rural results section [screen-detected AF during study]
OAC treatment (screened and unscreened): warfarin vs NOACs	Warfarin: 10% NOACs: 90%	Apportioned using a mean cost for NOACs	AF-SMART rural results [not published]
Screening participation rate	34%		AF-SMART rural results section
Cost per screen	\$20	Includes cost of eHealth tools and GP/nurse time (5min)	Based on the cost of recording a 12-lead ECG without interpretation (MBS item 11702 <sup>34</sup> )
Discount rate	5%		
<b>Follow-up costs for those with abnormal screening result [possible AF or unclassified]</b>			
12 lead ECG	\$31.75	1 per possible AF result  0.85 per unclassified result	MBS item 11700 <sup>34</sup>
GP visit (follow-up)	\$38.20	0.15 for each 12 lead ECG	MBS item 23 <sup>34</sup>
<b>Annual medication costs</b>			
Warfarin	\$238.83 per year	Warfarin 1mg + 3mg (once per day)	PBS dispensed price for maximum quantity <sup>35</sup>
Apixaban	\$1119.72 per year	2 tablets per day	PBS dispensed price for maximum quantity <sup>35</sup>
Dabigatran	\$1065.24 per year	2 tablets per day	PBS dispensed price for maximum quantity <sup>35</sup>
Rivaroxaban	\$1050.72 per year	1 tablet per day	PBS dispensed price for maximum quantity <sup>35</sup>
<b>Annual cost of monitoring/consults for those on OAC:</b>			
<b>Warfarin:</b>	<b>\$824.95 TOTAL</b>		
• GP visits	\$150.35 per year	3 GP visits per year (1 initial, 2 follow up)	MBS item 36 <sup>34</sup> = \$73.95 (initial) MBS item 23 <sup>34</sup> = \$38.20 (follow up)
• Specialist consult	\$155.60 per year	1 visit per year	MBS item 110 <sup>34</sup>
• INR monitoring	\$519 per year	30 INR tests per year	MBS item 65120 <sup>34</sup> , \$17.30 per test
<b>NOACs:</b>	<b>\$303.15 TOTAL</b>		
• GP visits	\$112.15 per year	2 GP visits per year (1 initial, 1 follow-up)	MBS item 36 <sup>34</sup> = \$73.95 (initial) MBS item 23 <sup>34</sup> = \$38.20 (follow up)
• Pathology	\$35.40 per year	2 per year	MBS item 66512 <sup>34</sup>

Item	Cost/measure	Details	Source
		(liver function, urea, electrolytes, creatinine tests)	\$17.70 per test
<ul style="list-style-type: none"> <li>Specialist consult</li> </ul>	\$155.60 per year	1 visit per year for all patients on OAC	MBS item 110 <sup>34</sup>
Other costs for those with diagnosed AF			
Echocardiogram	\$230.65	Once per patient	MBS item 55113 <sup>34</sup>
Stroke data			
Hospitalisation ischemic stroke	\$71,814 (first stroke) \$35,215 (recurrent stroke)	Includes hospitalisation, rehabilitation and other ongoing medical costs	Cadilhac et al, 2007 <sup>36</sup> updated to 2019 prices using Australian Health Price Deflator Index
QALYs per ischaemic stroke	5.09		Cadilhac et al, 2010 <sup>21</sup>
Annual incidences of stroke and all-cause mortality by age and sex			Martinez et al, 2014 <sup>37</sup>
Bleeding costs			
Crude excess incidence rate per 1,000 person-years of major bleeds for those aged 65 – 74 years	4.8 (95% CI: 2.2-7.4)		Martinez et al, 2014 <sup>37</sup>
Crude excess incidence rate per 1,000 person-years of major bleeds for those aged 75 – 84 years	4.2 (95% CI: 1.3-7.2)		Martinez et al 2014 <sup>37</sup>
Cost of a major gastrointestinal bleed	\$6,772		Australian Refined Diagnosis Related Groups (AR DRG) <sup>38</sup>
Cost of a major intracranial bleed	\$22,255		AR DRG <sup>38</sup>
Proportion of major bleeds: - gastrointestinal - intracranial	85% 15%		

AF, atrial fibrillation; iECG, smartphone electrocardiogram; OAC, oral anticoagulant; NOAC, novel oral anticoagulant; GP, general practitioner; ECG, electrocardiogram; PBS, pharmaceutical benefits scheme; MBS, medical benefits schedule; INR, international normalised ratio; QALYs, quality adjusted life years; \$ = AU\$, CI, confidence interval

The full model is available on request from the corresponding author.