Atrial Fibrillation Screen, Management And Guideline Recommended Therapy (AF

SMART II) in the rural primary care setting: a cross-sectional study and cost-

effectiveness analysis of eHealth tools to support all stages of screening

Short title: AF SMART II: AF screening in rural primary care

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1 Abstract

2 Background

3 Internationally, most atrial fibrillation (AF) management guidelines recommend

4 opportunistic screening for AF in people aged \geq 65 years, and oral anticoagulant (OAC)

5 treatment for those at high stroke risk (CHA₂DS₂-VA \geq 2). However, gaps remain in screening

6 and treatment.

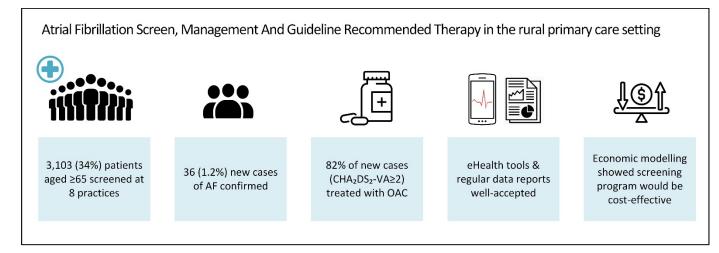
7 Methods and Results

8 General practitioners/nurses at practices in rural Australia(n=8) screened eligible patients 9 (aged \geq 65 years without AF) using a smartphone electrocardiogram during practice visits. 10 eHealth tools included electronic prompts, guideline-based electronic decision support, and 11 regular data reports. Clinical audit tools extracted deidentified data. Results were compared to an earlier study in metropolitan practices(n=8) and non-randomised control 12 13 practices(n=69). Cost-effectiveness analysis compared population-based screening to no 14 screening and included screening, treatment and hospitalisation costs for stroke and serious 15 bleeding events. Patients (n=3,103, 34%) were screened (mean age 75.1±6.8 years, 47% male) and 36(1.2%) new AF cases were confirmed (mean age 77.0 years, 64% male, mean 16 17 CHA₂DS₂-VA=3.2). OAC treatment rates for patients with CHA₂DS₂-VA≥2 were 82% (screendetected) versus 74% (pre-existing AF)(p=NS), similar to metropolitan and non-randomised 18 19 control practices. The incremental cost-effectiveness ratio (ICER) for population-based 20 screening was AU\$16,578/quality adjusted life year gained and AU\$84,383/stroke prevented compared to no screening. National implementation would prevent 147 21 strokes/year. Increasing the proportion screened to 75% would prevent 177 additional 22 23 strokes/year.

1 Conclusions

- 2 An AF screening program in rural practices, supported by eHealth tools, screened 34% of
- 3 eligible patients and was cost-effective. OAC treatment rates were relatively high at
- 4 baseline, trending upwards during the study. Increasing the proportion screened would
- 5 prevent many more strokes with minimal ICER change. eHealth tools, including data reports,
- 6 may be a valuable addition to future programs.
- 7 Clinical Trial Registration
- 8 URL: <u>www.anzctr.org.au</u>. Unique identifier: ACTRN12618000004268.
- 9 Keywords
- 10 Digital health, general practice, primary care, rural, stroke prevention, cost effectiveness
- 11

12 Graphical abstract



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1 Clinical Perspective

2 What is new?

3	•	This study extends the evidence base in rural areas by demonstrating that a screening
4		program using eHealth tools in the rural general practice setting can successfully screen 34%
5		of eligible atrial fibrillation (AF) patients with guideline-indicated treatment rates >80% for
6		screen-detected AF cases.
7	٠	Economic modelling showed the program was cost-effective compared to no screening.
8	٠	Oral anticoagulant (OAC) treatment rates for eligible patients were higher than previous
9		studies at baseline (>70%) and were trending upwards during the study (around 80%).
10	What a	are the clinical implications?
11	•	eHealth tools, particularly customised data reports as part of an audit and feedback system,
12		may be a valuable addition to screening programs
13	•	Half the practices screened 40-50% of eligible patients, suggesting this may represent a
14		'ceiling' of patients captured by opportunistic AF screening programs in the general practice
15		setting.
16	•	Increasing the proportion screened would prevent many more strokes with minimal change
17		to the incremental cost-effectiveness ratio (ICER).

1 Introduction

Internationally, opportunistic screening for atrial fibrillation (AF) in people aged ≥65 years is
now recommended by most guidelines.^{1, 2} Single-timepoint screening detects undiagnosed
AF, which is often asymptomatic, in approximately 1.4% of people in this age group.³
Guidelines generally recommend treatment with oral anticoagulants (OACs),^{1, 2} which can
reduce the risk of AF-related stroke by 64% for those at high risk ("sexless" CHA₂DS₂-VA risk
score ≥2).⁴

8 Large gaps in screening and treatment exist in practice. A survey conducted by The *Economist* in 2017 reported that only 11% of people aged ≥65 years were screened in 9 10 Australian general practices in the previous fortnight.⁵ Our previous 2018 study using 11 eHealth tools conducted in metropolitan general practices increased screening to 16% of eligible patients.⁶ In terms of treatment, rates have historically been 50-60%. However, 12 since non-vitamin K dependent OAC (NOAC) medicines were introduced, an increase in 13 14 treatment rates has been reported in Europe (>77% in England⁷ and >65% in Denmark⁸). 15 This trend was also reflected in our 2018 metropolitan study, which reported a treatment 16 rate of 71% for those diagnosed with AF prior to the study, increasing to >80% for those diagnosed during the study period.⁶ 17

Australians living in rural areas have more limited access to health services and worse cardiovascular outcomes.⁹ The ratio of 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.^{10, 11} Approximately 25% of the rural population suffers from cardiovascular diseases compared with 20% in metropolitan areas and the likelihood of hospitalisation and death resulting from cardiac events increases with the distance from

1	metropolitan areas. ¹² General practices play a key role in supporting cardiac health in rural
2	areas as they tend to provide a broader range of community services compared to
3	metropolitan practices. ¹³
4	Several of our previous studies showed opportunistic screening in primary care by general
5	practitioners (GPs) and nurses was feasible. ^{6, 14, 15} A suite of customised eHealth tools,
6	including an automated prompt and electronic decision support, were found to be
7	promising. ⁶ These tools have been refined and enhanced with a quality improvement (QI)
8	focus, ^{16, 17} and are designed to support all stages of screening.
9	This study aims to improve the proportion of patients screened and treated for AF using the
10	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

12 general practice.

13 Methods

11

This study was conducted in a convenience sample of 8 rural general practices from 14 September 2018-July 2019 in rural New South Wales, Australia. Practices were required to 15 16 be located outside a major city (generally categorised under the Australian Statistical Geography Standard - Remoteness Area ASGS-RA 2016¹⁸ code 2 "inner regional Australia") 17 18 and were recruited by advertisements in Primary Health Network newsletters and by wordof-mouth. Participating practices provided written informed consent and patients provided 19 20 oral consent for screening. This study was approved by the University of Sydney Human 21 Research Ethics Committee (Project no. 2017/1017). Clinical trial registration: 22 ACTRN12618000004268. The data and materials will not be made available to other 23 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.

3	The methods for this study have been previously described in detail. ¹⁷ Briefly, GPs and/or					
4	practice nurses offered screening for AF with smartphone handheld single lead					
5	electrocardiograms (iECGs) (KardiaMobile) to eligible patients attending the practice for any					
6	reason. Eligible patients were those aged ≥65 years without an existing AF diagnosis who					
7	had not already been screened with the iECG within the past 12 months. All follow-up for					
8	those with abnormal screening results according to the iECG app ("possible AF" or					
9	"unclassified") and treatment decisions were at the discretion of the GP.					
10	To support screening, practices were provided with the following eHealth tools (Figure 1):					
11	• Screening prompt: an app located in a third-party hosting platform automatically					
12	extracted information from patients' electronic medical records. Using this					
13	information in real-time, a prompt appeared when an eligible patient's file was					
14	opened. The iECG automated screening result was also recorded in this app.					
15	• Electronic decision support (EDS): for those diagnosed with AF (either by screening					
16	or otherwise), the EDS app (also located on the third-party hosting platform)					
17	calculated their CHA_2DS_2 -VA stroke risk score and made guideline recommendations					
18	regarding treatment. This app was part of the HealthTracker suite of cardiovascular					
19	quality improvement tools.					
20	• Tailored clinical audit data for QI reporting: customised, deidentified clinical audit					
21	data extracts were obtained monthly from participating practices. These data were					
22	used to report back to practices and included data on number and proportion					

screened, the number of patients with new AF and the proportion treated according
 to guidelines.

3

4 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.

10 Data collection and analysis

11 De-identified data extracts included demographic, iECG screening, medication and

12 diagnostic information from the practices' electronic patient records. The data extracts were

13 designed to collect data for all "active patients" of the practices, i.e. patients who had

14 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 15 16 study were compared with two other deidentified datasets: the "metropolitan group" and 17 the "non-randomised control group". These comparator datasets were collected from other Australian studies also using the HealthTracker app, with prospectively collected data using 18 19 the same data extraction tool and data fields. The metropolitan group was from our 2018 AF 20 screening study⁶ which included 8 metropolitan general practices. The non-randomised 21 control group was comprised of 69 practices (64 metropolitan and 5 rural) that were using HealthTracker for general cardiovascular QI studies that did not involve AF screening. For 22 the purposes of comparisons of treatment rates before and during the study period, the 23

non-randomised control group data were split into AF diagnoses prior to 1 January 2018
 (baseline treatment rate) and AF diagnosed on or later than 1 January 2018 (AF diagnosed
 during the study period).

Descriptive analyses for the rural practices were carried out using Microsoft Excel.
Descriptive analyses of non-randomised control data were performed using R Statistical
Programming, V3.6.1.¹⁹ Comparisons of treatment rates between groups were calculated
using Fisher's exact test (2-sided p-values) performed using 2x2 contingency tables
(GraphPad Prism V7.04, California, USA) with significance set a-priori at p<0.05. Although
our protocol paper specified a chi-square test, Fisher's 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 semi structured 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.¹⁶

16 Cost effectiveness analysis

The iECG screening program was evaluated by comparing population-based AF screening to no screening from an Australian health funder perspective. The economic model developed in the SEARCH-AF²⁰ pharmacy screening study was adapted to evaluate iECG screening in general practice. The model has previously been explained in detail.²⁰ 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 aged 65-84 years. That is, it compares population-based AF screening to no screening. It assumes a 'base rate'

1	of AF (both diagnosed and unknown) and follows a cohort of the population aged 65-84
2	years over 10 years with annual stroke events and all-cause mortality.
3	Stroke costs included hospitalisation, rehabilitation and other ongoing medical costs. For
4	this study, the model was updated to include the cost of an echocardiogram for those
5	diagnosed, the cost of major bleeding episodes for those on OAC treatment and a treatment
6	regimen consistent with current trends (i.e. including NOACs prescribed at rates observed in
7	the current study).
8	The model included the following key assumptions (full list included as Supplemental Table
9	1):
10	• The proportion screened was that observed in this study;
11	• The prevalence of diagnosed AF in the population aged ≥ 65 years was 4.4%; ³
12	• The prevalence of unknown AF in the population aged \geq 65years was 1.4%; ³
13	OAC and antiplatelet treatment rates were as observed for all patients diagnosed
14	during the study period (both screen-detected and otherwise detected);
15	• The iECG test sensitivity was 97% and specificity was 92%;
16	• The cost per screen was \$20; and
17	• For those diagnosed with AF, annual treatment and monitoring costs for those on
18	OAC were AU\$1063.78 = (warfarin) and AU\$1401.73 (mean cost for NOACs), and
19	included annual costs of medication, pathology, GP and specialist visits.
20	Costs for hospitalisation for stroke were obtained from Cadillhac et al ²¹ and were updated
21	to 2019 prices using the Australian Health Price Deflator Index. In addition, a present value
22	of 5.09 quality adjusted life years (QALYs) (gained over a lifetime) was used for each
23	ischemic stroke prevented by screening. ²¹

1	Results are presented in Australian dollars as an incremental cost-effectiveness ratio (ICER)					
2	per stroke avoided and per QALY gained for population-based screening compared to no					
3	screening. Sensitivity analyses were also performed for different proportions of patients					
4	screened, and for price reductions in NOAC medicines.					
5	Outcomes					
6	Key study outcomes were: ¹⁷					
7	• The proportion of screened patients with confirmed new AF					
8	• The proportion of AF and screened patients where the EDS was accessed					
9	• The proportion of AF patients diagnosed during the study period in the OAC					
10	recommended category (CHA ₂ DS ₂ -VA risk score ≥ 2) ¹ who were prescribed OAC					
11	according to guidelines					
12	 Baseline AF prevalence in patients aged ≥65 years compared to metropolitan and 					
13	non-randomised control groups					
14	• New screen-detected AF incidence at the end of the study period in patients aged					
15	≥65 years, compared to metropolitan and non-randomised control groups					
16	Rates of OAC and antiplatelet treatment at baseline and completion for patients in					
17	the OAC recommended category, compared to metropolitan and non-randomised					
18	control groups					
19						
20	Results					
21	Screening, diagnosis and treatment					

22 Eight general practices were recruited and screened a total of 3,103 eligible patients (mean

age 75.1 ± 6.8 years, 47% male) 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 4/8 practices screening >40% of eligible
patients (Figure 2). In general, screening was highest in the first 1-2 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.

10 In total, 36 (1.2%) new cases of screen-detected AF were confirmed (mean age 77.0 years, 64% male, mean CHA₂DS₂-VA=3.2) (Table 1). The proportion of screen-detected AF patients 11 with at least one non-age or gender risk factor was 83%, and the proportion in the OAC 12 13 recommended category (CHA₂DS₂-VA≥2) was 94%. Characteristics and CHA₂DS₂-VA groups 14 for those with screen-detected AF, otherwise-detected AF (during the study period) and 15 those with AF detected before the study are presented in Table 1. 16 OAC treatment rates of patients with AF with CHA₂DS₂-VA≥2 were 82% (screen-detected), 17 75% (otherwise-detected during study period) and 74% (pre-existing AF), with no significant differences between treatment rates in the screen-detected and other groups (Table 1). The 18

19 EDS was accessed for 54/1337 (4%) of all patients aged ≥65 with AF and for 4/36 (11%) of

20 new screen-detected AF patients.

1 AF prevalence and treatment rates compared with metropolitan and non-randomised

2 controls groups

3 The baseline prevalence of AF in the rural, metropolitan and practices and non-randomised

- 4 control groups ranged from 9-12% (Table 2).
- 5 There were no significant differences between the rural and metropolitan practices'
- 6 treatment rates of those with AF detected prior to the study or during the study (screen-
- 7 detected and otherwise-detected) (Table 2). Likewise, the treatment rates in the rural
- 8 practices were similar to those in the non-randomised control practices at baseline and
- 9 during the study period (Table 2). The OAC treatment rates in all 3 cohorts tended to
- 10 increase from baseline (Table 2), in contrast to antiplatelets.

11 Cost-effectiveness analysis

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

17 Increasing the screening participation rate has a negligible effect on the ICER but

18 substantially increases the number of strokes prevented, i.e. effectiveness (Table 3).

19 Increasing the screening participation rate from 34% to 50% raises the number of strokes

- 20 prevented from the base case of 147 per year to 216 per year (or 1467 to 2157 over 10
- 21 years). With a 75% screening participation rate, a total of 324 strokes are prevented each
- 22 year (or 3235 strokes over 10 years) when compared to the no screening scenario. For
- 23 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 to no screening.

3 Discussion

This study investigated the impact of an AF screening program in rural general practices
using a smartphone 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.

9 This study featured a unique suite of integrated, customised eHealth tools, to support all 10 stages of AF screening and treatment in general practice. These tools were refined following our metropolitan study,⁶ and included an automated screening prompt (with improved 11 visibility and reliability), an EDS app to guide treatment, deidentified data extracts and with 12 regular QI 'audit and feedback' reporting to practices. We are not aware of any other 13 studies that include tools to cover all stages of AF screening and treatment, including 14 15 customised feedback. In particular, the refined screening prompt and the improved QI reporting were useful and motivating for participating GPs and nurses.¹⁶ 16

17 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.⁶ 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 very 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 due to time constraints and technical issues (eg difficulty taking a

reading on some patients).¹⁶ 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 allocating sufficient staff time for screening. These are
discussed in detail in our qualitative realist evaluation.¹⁶

A recent study of AF screening in 184 Canadian practices was able to screen 42% of eligible
patients.²² In addition, a study from the Netherlands where patients aged ≥65 years were
screened in 10 general practices during influenza vaccination sessions captured 35% of
eligible patients, which is almost identical to our study.²³ These results suggest 40-50% 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 to historical Australian data, and increased during the study. The treatment rates were highest for screen-detected AF (>80%). These treatment rates and trends very similar to those in the non-randomised control practices. These rates are higher than previously reported in Australia, which were around 55-60%²⁴ prior to the introduction of NOACs (preferred by the Australian guidelines¹). Our results show a similar trend to recent European treatment rates of around 65%-80%^{8, 25, 26} since the introduction of NOACs.

Our results also show a decline in antiplatelet prescription for those not on OAC. Of the patients diagnosed during the study period (aged \geq 65 years with CHA₂DS₂-VA \geq 2) who were not prescribed OAC (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 alone, 2 of these patients were prescribed antiplatelets before being diagnosed with AF (one of whom had cardiovascular disease) and another 3 of these patients also had cardiovascular disease,

1	which may be the reason antiplatelets were prescribed. This suggests that prescription of
2	antiplatelet alone for AF may be declining, as was recently reported in a US study, ²⁷ and that
3	effectively the prescribing decision is becoming "OAC or no treatment".
4	Rural setting
5	This study extends the evidence base in rural areas and shows a screening program in the
6	rural general practice setting can successfully screen a large number of eligible AF patients
7	with guideline-indicated treatment rates over 80% for screen-detected AF cases. A
8	screening program using pulse palpation in rural general practice in Ireland achieved similar
9	reach to our study (30% of the general practice population aged ≥65 years screened)
10	although OAC treatment rates were lower (65%). ²⁸ The authors noted important differences
11	regarding the density of population in rural studies compared to metropolitan, with
12	implications for rural patients' access to primary and secondary care.
13	Prevention programs suitable for rural areas are particularly important, given that people
14	living in these areas tend to have worse cardiovascular outcomes and less access to
15	specialist medical services. ⁹ Rural general practice is potentially an ideal setting for
16	implementation of innovative primary care-based cardiac programs, such as ours, which
17	contribute to upskilling GPs in cardiac care, training nurses to provide cardiac
18	education/screening, and use of novel technology.

19 Cost-effectiveness

20 Our cost-effectiveness modelling showed that for population-based AF screening in general

21 practice for Australian men and women aged 65-84 years, the ICER per QALY gained was

AU\$16,578 and the ICER per stroke avoided was \$84,383 compared to no screening.

23 Increasing the proportion screened from 34% to 75% would prevent an additional 177

strokes per year (or 1,768 strokes over 10 years) with a negligible effect on the ICER. These
figures are higher than for SEARCH-AF,²⁰ largely driven by 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 accepted thresholds of
Australian government health expenditure.²⁹ This is consistent with several other studies,
which found AF screening to be cost-effective³⁰ or even cost-saving³¹.

8 Importantly, while we were able to screen 34% of eligible people with these tools (and have 9 suggested that 40-50% may be a 'ceiling' of patients captured with opportunistic screening 10 programs), these analyses highlight the impact of increasing the proportion screened in 11 terms of stroke prevention and the need to consider new approaches to break the 40-50% 12 barrier.

13 Limitations

14 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 15 substantially for practices, as was also noted in a recent Canadian study,²² as all of these 16 17 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 18 positives (e.g. due to sinus arrhythmia, multiple atrial ectopics or a poor quality trace). It is 19 20 also possible that some AF diagnoses were not recorded in the clinical system (see below). In relation to the 'unclassified' results, previous studies have usually reported lower rates 21 closer to 10%.^{6, 14} Improvements in the device algorithm (eg to identify sinus 22 23 tachycardia/bradycardia) and training staff in techniques to take clearer readings will reduce

this burden. We note the research team were 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%.²⁰

5 The EDS was only used for a low proportion of patients. This is probably because it was in a 6 separate app and was not accessed by GPs as it required extra clicks. Ideally, an EDS would 7 need to be a more integral part of the electronic medical record system. Alternatively, an 8 automatic calculation of patients' CHA₂DS₂-VA scores in the electronic medical record would 9 assist, particularly if it included an alert to review treatment when the score changed 10 (especially when it exceeds a treatment-recommendation threshold).

The study relied on deidentified data collected from practices. This was routinely collected 11 general practice data, with all its inherent limitations. For example, if GPs recorded a 12 13 diagnosis of AF in the free-text notes section instead of adding it as a condition from a drop-14 down list, this would not be caught in our data, meaning our figures may underestimate the 15 true rate of AF detected during the study. In addition, these data were limited to 'active patients' due to the definition in the data collection tool. 'Active patients' were defined as 16 those who had attended the practice at least three times in the past 2 years and once in the 17 last 6 months. Therefore, our data may be biased towards people with more chronic 18 19 conditions requiring more frequent attendance at the practice.

20 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. Half the practices screened 40-50% of eligible patients, suggesting 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 upwards
during the study. Increasing the proportion screened would prevent many more strokes
with minimal change to the ICER. This may require new methods to break through the
'ceiling' captured by numerous opportunistic programs. eHealth tools, particularly
customised data reports as part of an audit and feedback system, may be a valuable
addition to future screening programs.

8

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1 Disclosures

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- 6 Pfizer. LN reports speaker fees from Daiichi-Sankyo, grants and honoraria from Pfizer/BMS,
- 7 Bayer and Boehringer Ingelheim. RG, BK and AP report that the George Institute for Global
- 8 Health has ownership of a social enterprise (George Health Enterprises) that may seek to
- 9 commercialise some components of the tools used in this study.
- 10

11 References

Brieger D, Amerena J, Attia J, Bajorek B, Chan KH, Connell C, Freedman B, Ferguson C, Hall T,
 Haqqani H, Hendriks J, Hespe C, Hung J, Kalman JM, Sanders P, Worthington J, Yan TD and Zwar N.
 National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand:
 Australian Clinical Guidelines for the Diagnosis and Management of Atrial Fibrillation 2018. *Heart Lung Circ.* 2018;27:1209-1266.

Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC,
 Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B,
 Vardas P and Group ESCSD. 2016 ESC Guidelines for the management of atrial fibrillation developed
 in collaboration with EACTS. *Eur Heart J*. 2016;37:2893-2962.

Lowres N, Olivier J, Chao TF, Chen SA, Chen Y, Diederichsen A, Fitzmaurice DA, Gomez Doblas JJ, Harbison J, Healey JS, Hobbs FDR, Kaasenbrood F, Keen W, Lee VW, Lindholt JS, Lip GYH,

- Mairesse GH, Mant J, Martin JW, Martin-Rioboo E, McManus DD, Muniz J, Munzel T, Nakamya J,
- Neubeck L, Orchard JJ, Perula de Torres LA, Proietti M, Quinn FR, Roalfe AK, Sandhu RK, Schnabel RB,

Smyth B, Soni A, Tieleman R, Wang J, Wild PS, Yan BP and Freedman B. Estimated stroke risk, yield,

26 and number needed to screen for atrial fibrillation detected through single time screening: a

27 multicountry patient-level meta-analysis of 141,220 screened individuals. *PLoS Med*.

- 28 2019;16:e1002903.
- Hart RG, Pearce LA and Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke
 in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146:857-67.
- The Economist Intelligence Unit. Preventing stroke: Uneven progress. A global policy
 research programme. *The Economist*. 2017;Sept 21:1-28.
- 33 6. Orchard J, Neubeck L, Freedman B, Li J, Webster R, Zwar N, Gallagher R, Ferguson C and
- 34 Lowres N. eHealth Tools to Provide Structured Assistance for Atrial Fibrillation Screening,
- 35 Management, and Guideline-Recommended Therapy in Metropolitan General Practice: The AF -
- 36 SMART Study. J Am Heart Assoc. 2019;8:e010959.

1 7. Public Health England. CVD: Primary Care Intelligence Packs, NHS South Norfolk CCG. 2017 2 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/622956/NHS_East 3 Riding of Yorkshire CCG CVD intelligence pack.pdf accessed 23 October 2019. 4 Gadsbøll K, Staerk L, Fosbøl EL, Sindet-Pedersen C, Gundlund A, Lip GYH, Gislason GH and 8. 5 Olesen JB. Increased use of oral anticoagulants in patients with atrial fibrillation: temporal trends 6 from 2005 to 2015 in Denmark. Eur Heart J. 2017;38:899-906. 7 Australian Institute of Health and Welfare (AIHW). Cardiovascular Medicines and Primary 9. 8 Health Care: A Regional Analysis. 2010. 9 10. Australian Bureau of Statistics. Australian Social Trends: Doctors and Nurses (Report No. 10 4102.0) 2013: 11 https://www.abs.gov.au/AUSSTATS/abs@.nsf/Lookup/4102.0Main+Features20April+2013#p6 12 11. Hamilton S, Mills B, McRae S and Thompson S. Evidence to service gap: cardiac rehabilitation 13 and secondary prevention in rural and remote Western Australia. BMC Health Serv Res. 2018;18:64. 14 12. National Rural Health Alliance. Cardiovascular disease in rural Australia 15 2015: https://www.ruralhealth.org.au/sites/default/files/publications/cardiovascular-disease-fact-16 sheet-may-2015.pdf. 17 13. Australian Department of Health. National Strategic Framework for Rural and Remote Health 18 2016: https://www1.health.gov.au/internet/main/publishing.nsf/Content/national-strategic-19 framework-rural-remote-health. 20 Orchard J, Lowres N, Freedman SB, Ladak L, Lee W, Zwar N, Peiris D, Kamaladasa Y, Li J and 14. 21 Neubeck L. Screening for atrial fibrillation during influenza vaccinations by primary care nurses using 22 a smartphone electrocardiograph (iECG): A feasibility study. Eur J Prev Cardiol. 2016;23:13-20. 23 15. Orchard J, Freedman SB, Lowres N, Peiris D and Neubeck L. iPhone ECG screening by practice 24 nurses and receptionists for atrial fibrillation in general practice: the GP-SEARCH qualitative pilot 25 study. Aust Fam Physician. 2014;43:315-9. 26 16. Orchard J, Li J, Gallagher R, Freedman B, Lowres N and Neubeck L. Uptake of a primary care 27 atrial fibrillation screening program (AF-SMART): a realist evaluation of implementation in 28 metropolitan and rural general practice. BMC Fam Pract. 2019;20:170. 29 17. Orchard JJ, Neubeck L, Freedman B, Webster R, Patel A, Gallagher R, Li J, Hespe CM, 30 Ferguson C, Zwar N and Lowres N. Atrial Fibrillation Screen, Management And Guideline 31 Recommended Therapy (AF SMART II) in the rural primary care setting: an implementation study 32 protocol. BMJ Open. 2018;8:e023130. 33 18. Australian Government. Australian Statistical Geography Standard - Remoteness Area. 34 2019:https://www.health.gov.au/health-workforce/health-workforce-classifications/australian-35 statistical-geography-standard-remoteness-area accessed 11 December 2019. 36 R Core Team. A language and environment for statistical computing. R Foundation for 19. 37 Statistical Computing 2019:Vienna, Austria. https://www.R-project.org/. 38 Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, Bennett AA, Briffa T, 20. 39 Bauman A, Martinez C, Wallenhorst C, Lau JK, Brieger DB, Sy RW and Freedman SB. Feasibility and 40 cost-effectiveness of stroke prevention through community screening for atrial fibrillation using 41 iPhone ECG in pharmacies. The SEARCH-AF study. Thromb Haemost. 2014;111:1167-76. 42 21. Cadilhac DA, Dewey HM, Vos T, Carter R and Thrift AG. The health loss from ischemic stroke 43 and intracerebral hemorrhage: evidence from the North East Melbourne Stroke Incidence Study 44 (NEMESIS). Health Qual Life Outcomes. 2010;8:49. 45 22. Godin R, Yeung C, Baranchuk A, Guerra P and Healey JS. Screening for Atrial Fibrillation Using 46 a Mobile, Single-Lead Electrocardiogram in Canadian Primary Care Clinics. Can J Cardiol. 47 2019;35:840-845. 48 23. Kaasenbrood F, Hollander M, Rutten FH, Gerhards LJ, Hoes AW and Tieleman RG. Yield of 49 screening for atrial fibrillation in primary care with a hand-held, single-lead electrocardiogram device 50 during influenza vaccination. *Europace*. 2016;18:1514-1520.

Alamneh EA, Chalmers L and Bereznicki LR. The Tasmanian atrial fibrillation study: Transition
 to direct oral anticoagulants 2011-2015. *Cardiovasc Ther*. 2017;35:e12254.

Cowan JC, Wu J, Hall M, Orlowski A, West RM and Gale CP. A 10 year study of hospitalized
atrial fibrillation-related stroke in England and its association with uptake of oral anticoagulation. *Eur Heart J.* 2018;39:2975-2983.

Rodríguez-Bernal CL, Hurtado I, García-Sempere A, Peiró S and Sanfélix-Gimeno G. Oral
 Anticoagulants Initiation in Patients with Atrial Fibrillation: Real-World Data from a Population-Based
 Cohort. Front Pharmacol. 2017;8:63.

Maggioni AP, Dondi L, Andreotti F, Pedrini A, Calabria S, Ronconi G, Piccinni C and Martini N.
 Four-year trends in oral anticoagulant use and declining rates of ischemic stroke among 194,030

11 atrial fibrillation patients drawn from a sample of 12 million people. *Am Heart J.* 2019.

12 28. Smyth B, Marsden P, Corcoran R, Walsh R, Brennan C, McSharry K, Clarke J, Kelly PJ and 13 Harbison J. Opportunistic screening for atrial fibrillation in a rural area. *QJM*. 2016;109:539-543.

14 29. Edney LC, Haji Ali Afzali H, Cheng TC and Karnon J. Estimating the Reference Incremental

15 Cost-Effectiveness Ratio for the Australian Health System. *Pharmacoeconomics*. 2018;36:239-252.

16 30. Freedman B, Camm J, Calkins H, Healey JS, Rosenqvist M, Wang J, Albert CM, Anderson CS,

Antoniou S, Benjamin EJ, Boriani G, Brachmann J, Brandes A, Chao TF, Conen D, Engdahl J, Fauchier
 L, Fitzmaurice DA, Friberg L, Gersh BJ, Gladstone DJ, Glotzer TV, Gwynne K, Hankey GJ, Harbison J,

Hillis GS, Hills MT, Kamel H, Kirchhof P, Kowey PR, Krieger D, Lee VWY, Levin LA, Lip GYH, Lobban T,

Lowres N, Mairesse GH, Martinez C, Neubeck L, Orchard J, Piccini JP, Poppe K, Potpara TS,

21 Puererfellner H, Rienstra M, Sandhu RK, Schnabel RB, Siu CW, Steinhubl S, Svendsen JH, Svennberg E,

22 Themistoclakis S, Tieleman RG, Turakhia MP, Tveit A, Uittenbogaart SB, Van Gelder IC, Verma A,

23 Wachter R, Yan BP and Collaborators AF-S. Screening for Atrial Fibrillation: A Report of the AF-

24 SCREEN International Collaboration. *Circulation*. 2017;135:1851-1867.

Jacobs MS, Kaasenbrood F, Postma MJ, van Hulst M and Tieleman RG. Cost-effectiveness of
 screening for atrial fibrillation in primary care with a handheld, single-lead electrocardiogram device
 in the Netherlands. *Europace*. 2018;20:12-18.

28

1 Figure legends

- **Figure 1** Screening process and eHealth tools adapted from our 2018 metropolitan study⁶
- **Figure 2** Screening flowchart

- 1 Tables
- 2 Table 1
- 3

4 Table 1 – characteristics and stroke risk of those with AF aged \geq 65 years

	Screen-detected	Otherwise-	Baseline: AF
	AF	detected AF	diagnosed
		during study	before study
		period	
	(n=36)	(n=58)	(n=1243)
Age in years (mean ± SD)	77.0 ± 6.1	77.0 ± 8.4	79.2 ± 7.8
Male, n (%)	23 (64%)	32 (55%)	662 (53%)
Mean CHA ₂ DS ₂ -VA	3.2	3.3	3.7
CHA ₂ DS ₂ -VA ≥2, n (% of total)	34 (94%)	55 (95%)	1223 (98%)
CHA_2DS_2 -VA ≥ 2 and prescribed	28 (82%)	41 (75%)	908 (74%)
OAC, n (% of those with CHA_2DS_2 -		p=0.444†	p=0.326†
VA ≥2)			
≥1 non-age or gender risk factors,	30 (83%)	54 (93%)	1178 (95%)
n (% of total)			

- 5 AF, atrial fibrillation; SD, standard deviation; CHA₂DS₂-VA: C, congestive heart failure/left
- 6 ventricular dysfunction; H, high blood pressure; A₂, age >75 years; D, diabetes; S₂,
- 7 stroke/transient ischemic attack/thromboembolism; V, vascular disease [coronary artery
- 8 disease, myocardial infarction, peripheral artery disease, aortic plaque]; A, age 65 74
- 9 years; † p-value for comparison to screen-detected AF

1 Table 2

2

3 Table 2: Treatment rates and comparisons between groups: patients aged ≥65 years with

4 **AF**

	Rural	Metropolitan	Non-randomised
	practices	practices	control practices
	(n=8)	(n=8)	(n=69)
Total active* patients aged ≥65 years	10,896	13,679	30,116
Baseline AF prevalence	12%	11%	9%
Baseline: AF detected prior to study w	ith CHA ₂ DS ₂ -V/	A≥2	
Total, n	1223	1306	1875
Prescribed OAC, n (%)	908 (74%)	933 (71%)	1450 (77%)
		p=0.118†	p=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 perio	d with CHA₂DS	5₂-VA≥2	
Total, n	34	18	N/A
Prescribed OAC, n (%)	28 (82%)	15 (83%)	N/A
		p>0.999†	
Prescribed antiplatelet alone, n (%)	1 (3%)	1 (6%)	N/A
Not prescribed OAC or antiplatelet, n	5 (15%)	2 (11%)	N/A
(%)			
	1		

	Rural practices (n=8)	Metropolitan practices (n=8)	Non-randomised control practices (n=69)
All AF detected during study period (so	reen-detected +	otherwise-detecte	d) with CHA ₂ DS ₂ -
VA≥2			
Total, n	89	64	399
Prescribed OAC, n (%)	69 (78%)	54 (84%)	333 (83%)
		p=0.312†	p=0.218†
Prescribed antiplatelet alone, n (%)	7 (8%)	3 (5%)	29 (7%)
Not prescribed OAC or antiplatelet, n	13 (15%)	7 (11%)	37 (9%)
(%)			

1 *active patients are those who attended the practice at least 3 times in the last 2 years and

2 once in the last 6 months

3 + p-value for comparison to rural practices

4 AF, atrial fibrillation; OAC, oral anticoagulant; CHA₂DS₂-VA: C, congestive heart failure/left

5 ventricular dysfunction; H, high blood pressure; A₂, age >75 years; D, diabetes; S₂,

6 stroke/transient ischemic attack/thromboembolism; V, vascular disease [coronary artery

7 disease, myocardial infarction, peripheral artery disease, aortic plaque]; A, age 65 – 74

8 years.

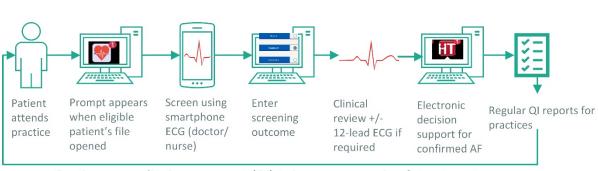
1 Table 3

2 Table 3: Cost effectiveness of population-based AF screening compared to no screening

3 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 to no	\$84,383	\$83,304	\$82,922	\$82,649	\$82,540
screening					
Net cost [ICER] per QALY					
gained compared to no	\$16,578	\$16,366	\$16,291	\$16,238	\$16,216
screening					
NOAC price reduction	-	12.5%	25%		
Screening participation rate	34%	34%	34%		
Number of strokes prevented	1467	1467	1467		
Net cost [ICER] per stroke					
prevented compared to no	\$84,383	\$76,336	\$68,289		
screening					
Net cost [ICER] per QALY					
gained compared to no	\$16,578	\$14,997	\$13,416		
screening					

- 1 ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year; NOAC, novel
- 2 anticoagulant; \$ = AU\$
- 3
- 4
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- 5 Figures
- 6 Figure 1
- 7
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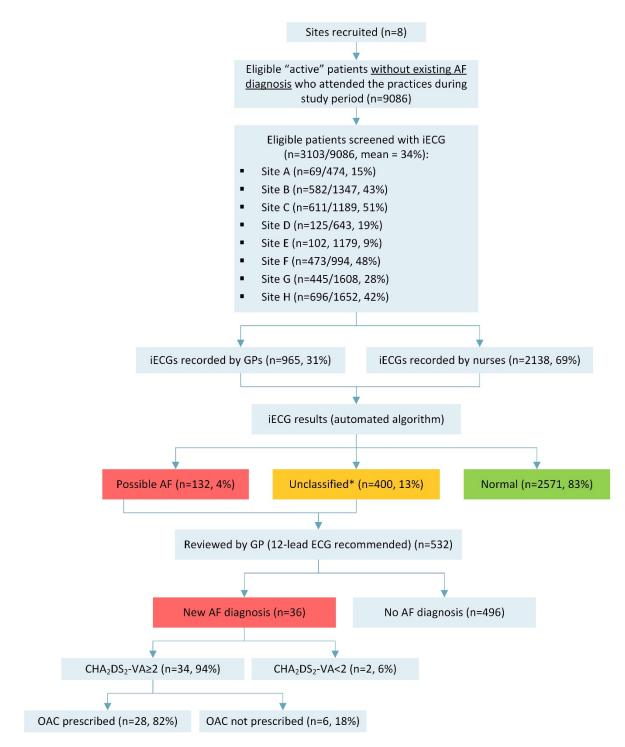
AF-SMART screening process

9

Continuous quality improvement (QI) to improve screening & treatment

10 **Figure 1** – Screening process and eHealth tools adapted from our 2018 metropolitan study⁶

1 Figure 2



* Unclassified results may be due to sinus bradycardia, sinus tachycardia, left or right bundle branch block, multiple ectopic beats or other arrhythmias

2

3 Figure 2 – Screening flowchart