Quarterly versus annual ECG screening for atrial fibrillation in older Chinese individuals (AF-CATCH): a prospective, randomised controlled trial

Wei Zhang, Yi Chen*, Chao-Ying Miao, Qi-Fang Huang, Chang-Sheng Sheng, Shuai Shao, Dian Wang, Shao-Kun Xu, Lei Lei, Di Zhang, Yi-Lin Chen, Lei-Xiao Hu, Jia-Hui Xia, Xiao-Fei Ye, Yi-Bang Cheng, Ying Wang, Qian-Hui Guo, Yan Li, Nicole Lowres, Ben Freedman, Ji-Guang Wang, for the AF-CATCH Investigators and Coordinators*

Summary

Background Screening for atrial fibrillation before onset of symptoms and the subsequent initiation of oral anticoagulants could prevent stroke and death. The most cost-effective strategy to screen for atrial fibrillation in a population at high risk aged 65 years and older is unknown. Therefore, we aimed to investigate whether more frequent electrocardiography (ECG) recordings would significantly improve the detection of atrial fibrillation compared with annual ECG screenings.

Methods We did a randomised controlled trial that compared different screening frequencies of 30 s single-lead ECG (AliveCor Heart Monitor) in the detection of atrial fibrillation in Chinese residents (≥65 years) in five community health centres in Shanghai, China. Only participants without history of atrial fibrillation and without atrial fibrillation rhythm at baseline were eligible for inclusion in the trial. Random assignment was done with the use of a random number table and stratified for study site. Participants were randomly assigned in a 1:1 ratio to annual or quarterly screening groups. The quarterly screening group was further randomly assigned in a 3:1 ratio to subgroups of quarterly screening and quarterly screening plus (which involved ECG screening once per week for the first month of follow-up, then quarterly for the remainder of follow-up). The primary outcome was the detection rate of atrial fibrillation. The intention-to-treat analysis was done for all randomly assigned patients who had at least one ECG recording during follow-up. This trial was registered at ClinicalTrials.gov, NCT02990741, and terminated on Oct 31, 2020.

Findings Between April 17, 2017, and June 26, 2018, 8240 participants were randomly assigned to annual screening (n=4120), quarterly screening (n=3090), and quarterly screening plus (n=1030), with a mean number of ECG recordings of 1·6 (SD 0·5) for annual screening, 3·5 (1·5) for quarterly screening, and 5·2 (2·9) for quarterly screening plus during a median of 2·1 years follow-up (13 284 person-years). 73 incident cases of atrial fibrillation occurred: 26 in the annual screening group (4·1 per 1000 person-years) and 47 in the quarterly screening group (6·7 per 1000 person-years. Quarterly screening was associated with a significant increase in the detection rate of atrial fibrillation, compared with annual screening (hazard ratio [HR] 1·71; 95% CI 1·06–2·76; p=0·029). 40 incident cases were detected in quarterly screening (7·2 per 1000 person-years; HR compared to annual screening, 1·83; 95% CI 1·12–3·00; p=0·017) and seven in the quarterly screening plus group (4·8 per 1000 person-years; HR compared with annual screening, 1·24; 0·54–2·86; p=0·61). No significant difference was noted between quarterly screening and the quarterly screening plus group (HR of quarterly screening plus compared with quarterly screening, 0·68; 0·30–1·52; p=0·35).

Interpretation Quarterly 30 s single-lead ECG screening was associated with a significantly higher detection rate of incident atrial fibrillation compared with annual screening, but additional once per week screenings in the first month did not yield an added predictive value. Quarterly screening might be considered in a general population at a high risk of atrial fibrillation, such as those aged 65 years and older.

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*Co-first authors

Department of Cardiovascular Medicine, Centre for Epidemiological Studies and Clinical Trials, Shanghai Key Laboratory of Hypertension, The Shanghai Institute of Hypertension, Shanghai, China (W Zhang MD, Y Chen PhD, C-Y Miao MD, Q-F Huang PhD, C-S Sheng PhD, S Shao PhD, D Wang PhD, S-K Xu PhD, L Lei MD, D Zhang MD, Y-L Chen MD, L-X Hu MD, J-H Xia MD, X-F Ye MSc, Y-B Cheng PhD, Y Wang MD, Q-H Guo PhD, Prof Y Li PhD, Prof J-G Wang PhD); **Department of Hypertension, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China** (W Zhang, Y Chen, C-Y Miao, Q-F Huang, C-S Sheng, S Shao, D Wang, S-K Xu, L Lei, D Zhang, Y-L Chen, L-X Hu, J-H Xia, X-F Ye, Y-B Cheng, Y Wang, Q-H Guo, Prof Y Li, Prof J-G Wang); **Heart Research Institute, Sydney Medical School, Charles Perkins Center, and Cardiology Department, Concord Hospital, The University of Sydney, Sydney, NSW, Australia** (N Lowres PhD, Prof B Freedman PhD)

Correspondence to: Prof Ji-Guang Wang, Department of Cardiovascular Medicine, Centre for Epidemiological Studies and Clinical Trials, Shanghai Key Laboratory of Hypertension, The Shanghai Institute of Hypertension, Shanghai 200025, China **jiguangwang@aim.com**

Introduction

The prevalence of atrial fibrillation in adults was estimated to be between 2% and 4% in 2019,[1] and is expected to rise by 2·3 times by 2060 because of increased longevity.[2,3] Atrial fibrillation is associated with a nearly five times increase in the risk of ischaemic stroke[4,5] and is often asymptomatic. In fact, asymptomatic atrial fibrillation is common[6] and, similar to symptomatic atrial fibrillation, has been independently associated with an increased risk of stroke and mortality.[7–10] Treatment

Research in context

Evidence before this study

Atrial fibrillation is a common heart rhythm problem that often has no symptoms, and is therefore often underdiagnosed. The early detection of asymptomatic atrial fibrillation and the subsequent initiation of appropriate treatment with oral anticoagulants could prevent stroke and death. There is little evidence to support the use of a widespread systematic approach to atrial fibrillation screening in populations at high risk. However, several studies have shown that multiple electrocardiography (ECG) recordings with handheld single-lead devices help to improve the detection of atrial fibrillation. The STROKESTOP study showed an increased detection rate from 0·5% on the initial ECG to 3·0% with 2 weeks of twice per day intermittent systematic screenings. The REHEARSE-AF study showed a higher yield of 3·8% using one to two 30 s single-lead ECG recordings per week over 1 year. Although repeated recordings also increase the cost of screening, the optimal frequency of monitoring is undefined.

Added value of this study

This randomised controlled trial showed that quarterly 30 s single-lead ECG screening significantly increased the detection rate of atrial fibrillation compared with annual ECG screening in older Chinese individuals, although additional once per week screening in the first month did not yield an added predictive value. Considering the low rate of oral anticoagulant therapy in patients with atrial fibrillation in China, whether this more intensive screening strategy could be widely recommended requires further investigation across a larger geographical area and in a larger population.

Implications of all the available evidence

To our knowledge, this study is the first randomised controlled trial that has investigated the use of 30 s single-lead ECG screening of various frequencies in the detection of atrial fibrillation in a population sample. This study contributed data on exploring an effective strategy to screen for atrial fibrillation in populations at high risk aged 65 years and older. Our study also revealed a serious public health issue in China, with the undertreatment of atrial fibrillation in the community. To prevent atrial fibrillation-related stroke, effort should be made to improve the use of oral anticoagulants in individuals with known atrial fibrillation, before more frequent or intensive screening for new atrial fibrillation can be recommended in China.

with oral anticoagulants (OACs) reduces the risk of ischaemic stroke by 64–70%.[11] Therefore, the early detection of asymptomatic atrial fibrillation and the subsequent initiation of appropriate OACs could prevent stroke and death.[12]

See Online for appendix

Current guidelines recommend opportunistic atrial fibrillation screening in populations at high risk.[13] Widespread systematic screening is not recommended because there are few studies that assess the efficacy of systematic screening. The clinical setting for atrial fibrillation screening varies between different countries and health-care systems.[14–18] Although taking repeated electrocardiography (ECG) recordings will result in a higher yield of atrial fibrillation diagnoses than taking single recordings, the appropriate frequency of monitoring, whether through the use of smartphones, watches, or any other techniques, is undefined. Defining the optimal number of ECG recordings in terms of cost-effectiveness requires further investigation. We describe the main results of the intensive versus usual ECG screening for Atrial Fibrillation in elderly Chinese by an Automated ECG sysTem in Community Health centres in Shanghai (AF-CATCH) study, a trial that was designed to investigate whether more frequent ECG recordings would significantly improve the detection of atrial fibrillation compared with annual ECG screenings in Chinese patients aged at least 65 years in community health centres.

Methods

Study design and participants

This study was a 2-year randomised controlled trial that compared quarterly ECG screening with annual ECG screening in the detection of atrial fibrillation in five community health centres in Shanghai. Details of the study protocol have been described previously in English,[19] and the protocol is available in the appendix (pp 9–13). During the trial, we had three time amendments to the protocol, with the documentation in Chinese.

We recruited residents aged 65 years or older from five community health centres (Yuyuan Community Health Centre, Laoximen Community Health Centre, Ruijin Second Road Community Health Centre, Sanlin Community Health Centre, and Kangde Community Health Centre) in urban areas of Shanghai, China. To recruit participants, the screening programme was publicised through a public health press conference and media release in Shanghai, official notices of the neighbourhood committee, and posters in the 5 above-mentioned community health centres. All residents aged 65 years or older were eligible for baseline assessment. Those without a history of atrial fibrillation and without atrial fibrillation rhythm at baseline were eligible for inclusion in the trial. Patients with serious life-threatening diseases, such as cancer or severe cardiovascular, cerebrovascular, liver, or kidney diseases, who might not manage to attend follow-up were excluded from the trial. Written informed consent was obtained from all study participants at the baseline screening clinic visit. All the amended protocols were approved by the Ethics Committee of Ruijin Hospital, Shanghai Jiaotong University School of Medicine. Our study was done in accordance with the principles of the Declaration of Helsinki.

Randomisation and masking

Eligible and consenting participants were randomly assigned in a 1:1 ratio to either the annual screening group or the quarterly screening group. Those within the quarterly screening group were further randomly assigned in a 3:1 ratio to subgroups of either quarterly screening or quarterly screening plus (ECG once per week for the first month of follow-up, then quarterly for the remainder of follow-up). Randomisation was done by an independent statistician (X-FY) with the use of a random number table and stratified for study site. There was no masking to screening assignments.

Procedures

During the baseline assessment visit at the community health centre, a single-lead (lead 1) ECG was recorded for 30 s with a handheld ECG device (AliveCor Heart Monitor, now Kardia Mobile, Mountain View, CA, USA). Each ECG rhythm strip was reviewed by a cardiologist from the research team (YC or WZ) at baseline screening visit. The ECGs were classified into three groups: sinus rhythm, atrial fibrillation, and uninterpretable. Participants with an uninterpretable single-lead ECG were referred for 12-lead ECGs, which were reviewed by a second cardiologist (DW or J-GW). Both atrial fibrillation and atrial flutter diagnosed by the ECG were classified as atrial fibrillation. A screening questionnaire (appendix p 4) regarding medical history, lifestyle behaviours (ie, smoking, alcohol intake), and the use of medications was given to all participants by the research cardiologists at baseline only. Participants with a history of atrial fibrillation (ie, a documented history of atrial fibrillation in their medical records from qualified hospitals or with atrial fibrillation recorded on any previous ECG) and who were in sinus rhythm on the screening ECG, were defined as having known atrial fibrillation in sinus rhythm and excluded. ECGs and medical records obtained outside the study centre were documented for verification.

Eligible participants were randomly assigned to groups of annual screening, or quarterly screening. Those participants who were enrolled into the quarterly screening group were then randomly assigned 3:1 into either quarterly screening or quarterly screening plus. In the annual screening group, ECG recordings were taken at annual follow-up visits at 12 and 24 months, for a total of two ECG recordings. In the quarterly screening subgroup, ECG recordings were taken quarterly during follow-up, at months 3, 6, 9, 12, 15, 18, 21, and 24, for eight ECG recordings in total. In the quarterly screening plus subgroup, ECG recordings were taken once per week during the first month of follow-up and quarterly thereafter, at weeks 1, 2, 3, and 4, and months 3, 6, 9, 12, 15, 18, 21, and 24, for 12 ECG recordings in total.

Every participant in the quarterly screening and quarterly screening plus group was given a schedule of follow-up visits. At every scheduled follow-up visit, a follow-up questionnaire (appendix p 7) was also administered, in addition to the ECG recording (which was also given to participants in the annual screening group). The follow-up questionnaire included the participants' survival status (if the participant was dead, their family member helped to complete the questionnaire, and we further searched information in the vital statistics database), newly diagnosed diseases, and adverse outcomes during follow-up. If participants did not attend the community health centre for ECG screens at the scheduled time, the research team would remind them by telephone. If participants were unable to attend the end-of-study visit in the community health centre at the 2-year follow-up, telephone follow-ups were offered.

The atrial fibrillation questionnaire (appendix pp 5–6), including the specific history of atrial fibrillation and treatment, was administered to participants with known and new atrial fibrillation at baseline screening, and participants with newly detected atrial fibrillation during follow-up. All participants with newly detected atrial fibrillation and participants with untreated known atrial fibrillation (who were excluded from the trial) were included in an educational intervention programme, which included a one-on-one disease educational intervention programme (involving one-on-one disease education with the research cardiologist at the community health centre and provision of educational materials, involving information on risk of stroke associated with atrial fibrillation, the appropriate treatment options of atrial fibrillation, and benefits and risks of anticoagulants, as well as information on how to make an appointment at a designated specialist clinic near each community) and advice to attend a specialist clinic for consultation and OAC prescription.[20] We aimed to improve oral anticoagulants prescription in patients with actionable atrial fibrillation by an educational intervention, to finally reduce the risk of atrial fibrillation-related strokes.

Outcomes

The primary outcome was the detection rate of atrial fibrillation, which included new screen-detected atrial fibrillation in the trial and clinically detected atrial fibrillation, because we think it is necessary to include both clinically detected and screen-detected atrial fibrillation, similar to a previously published cluster randomised controlled trial that included all incident atrial fibrillation in their primary analyses.[14] Clinically detected atrial fibrillation was defined as a clinical diagnosis of atrial fibrillation identified from an ECG recording outside of the trial, or identified as a result of symptoms or from presentation to hospital.

Other exploratory clinical outcomes included death from any cause, death from cardiovascular cause, non-fatal ischaemic or haemorrhagic stroke, acute coronary syndrome, and uncontrolled hypertension. Information about these clinical outcomes was collected at each clinic

follow-up visit and, for those who did not attend the clinic visit, by telephone calls. The diagnosis was verified against medical records and discharge summaries from qualified hospitals. We also checked the vital statistics of the Shanghai Municipal Centre for Disease Control and Prevention to ascertain the causes of death.

Statistical analysis

The rate of the newly detected atrial fibrillation by a single timepoint ECG recording was estimated to be 2·0% in older people (60 years or older) in Shanghai according to a previous study.[21] In a cluster randomised trial done in the UK,[14] systematic screening (an invitation for ECG) or opportunistic screening (pulse taking and an invitation for an ECG if the pulse was irregular) increased the detection rate of atrial fibrillation by 57%, from 1·04 to 1·63%. We therefore hypothesised that the detection rate could be improved by approximately 50% with quarterly ECG recordings compared with annual ECG recordings. Assuming a one-sided α=0·05, power of 80%, a one-sided test and a 1:1 ratio to assign patients to annual and quarterly ECG screenings, the study was calculated to require a sample size of 3013 participants per group. In consideration of a 15% dropout rate, we aimed to enrol 3500 eligible participants per group. The quarterly ECG screening plus subgroup is exploratory. The sample size of this subgroup was arbitrarily defined as 875 participants (ie, a quarter of the total number of participants in the quarterly ECG screening group). Therefore, the number of patients required would be 7000 in total: 3500 in the annual screening group, 2625 in the quarterly screening group, and 875 in the quarterly screening plus group.

The primary comparison was between the annual screening group and the quarterly screening group. An exploratory comparison was done between the quarterly screening subgroup and quarterly screening plus subgroup, and between annual, quarterly ECG recordings, and once per week ECG recordings. Predefined subgroup analyses were done according to sex, age (65–74 years *vs* ≥75 years), body-mass index (BMI; ≤25 kg/m² *vs* >25 kg/m²), or hypertension. Ad-hoc analyses were done for the presence of diabetes and history of cardiovascular disease.

Analyses were done in the intention-to-treat principle population, ie, all randomly assigned patients who had at least one ECG recording during follow-up. Age, BMI, systolic and diastolic blood pressure, and pulse rate at baseline were compared between the randomly assigned groups using ANOVA. Differences between groups in sex, current smoking status, alcohol intake, hypertension, diabetes, and a history of cardiovascular disease at baseline were assessed using χ^2 tests. A log-rank test was used to compare the cumulative incidence of atrial fibrillation between the groups, using the Kaplan-Meier survival function to show the time to event. Cox regression analysis was used to compute hazard ratios (HRs) for the detection rate of atrial fibrillation or other clinical outcomes. Predefined subgroup analyses were done according to sex, age (65–74 years *vs* ≥75 years), BMI (≤25 kg/m² *vs* >25 kg/m²), and the presence of hypertension, diabetes, and a history of cardiovascular disease to assess differences in detection between the annual and quarterly screening groups. SAS version 9·4 was used for data management and statistical analysis. Participants were censored at the last follow-up visit, if they did not develop new atrial fibrillation.

The trial is registered with ClincialTrials.gov, NCT02990741.

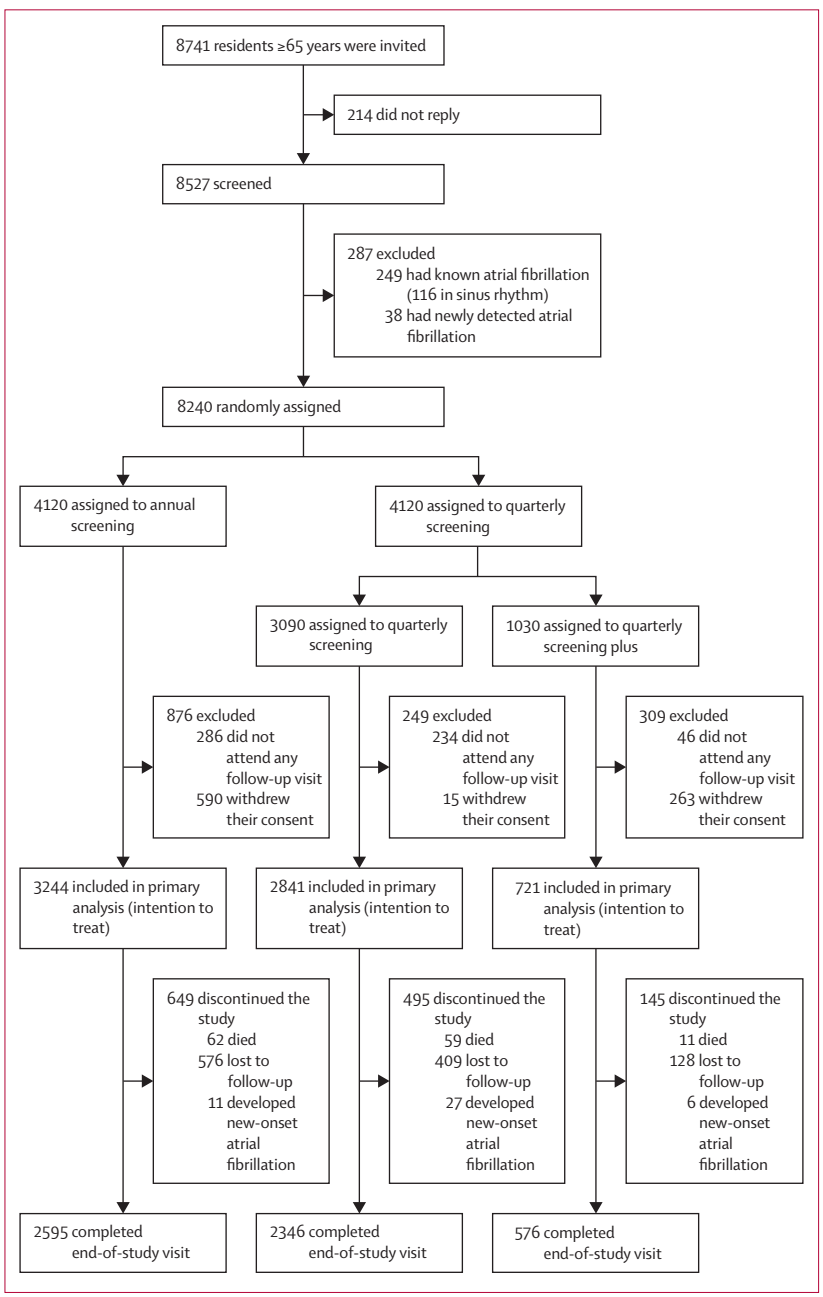

Figure 1: **Trial profile**

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

8741 residents aged 65 years or older attended the participating community health clinics from April 17, 2017, to June 26, 2018, and were invited to participate in the study, of whom 214 declined. 8527 adults (97·6%) participated in baseline assessment (figure 1). At baseline, the prevalence of atrial fibrillation was 3·4% (n=287), including 0·4% with previously unknown atrial fibrillation confirmed by an ECG (n=38), 1·6% with ECG-confirmed known atrial fibrillation (n=133), and 1·4% with known atrial fibrillation in sinus rhythm (n=116; appendix p 3). 8240 participants without a history of atrial fibrillation and atrial fibrillation rhythm and who did not meet any other exclusion criterion were randomly assigned to annual screening (n=4120), quarterly screening (n=3090), or quarterly screening plus (n=1030).

After the exclusion of 868 participants who withdrew their consent and 566 participants who did not attend any follow-up visit, 6806 participants were included in the primary analysis (figure 1 and table 1). The mean age of participants was 71·4 years (SD 6·2), 2982 (44%) were men, and 3824 (56%) were women. The baseline characteristics including age, sex, BMI, blood pressure, presence or absence of hypertension, or diabetes and history of cardiovascular disease were comparable between the three screening groups (table 1).

End-of-study visits were completed by Oct 31, 2020. 5517 participants completed their end-of-study visits (81·1% of the 6806 participants who completed at least one follow-up visit). The mean number of follow-up visits was 1·6 (SD 0·5) in the annual screening group, 3·5 (1·5) in the quarterly screening group, and 5·2 (2·9) in the quarterly screening plus group (p<0·0001]; table 2). Among participants in the annual screening group, 3244 (100%) completed at least one yearly visit and 1855 (57%) completed both yearly visits. Of the 2841 participants in the quarterly screening group, 2572 (91%) completed one or more quarterly visits, 2009 (71%) completed two or more, 1359 (48%) completed three or more, and 681 (24%) completed four or more. The adherence was similar across each of the quarterly follow-up visits, with an average of approximately 40% (28·6–57·9%). Of the 721 participants in the quarterly screening plus group, 429 (60%) completed one or more weekly visits, 362 (50%) completed two or more, 299 (41%) completed three or more, and 204 (28%) completed all four visits.

During a median of 2·1 (IQR 2·0–2·2) years of follow-up and a total of 13 284 person-years, incident atrial fibrillation was confirmed in 73 participants (43 screen-detected and 30 clinically detected): 26 in the annual screening group (4·1 per 1000 person-years; 95% CI 2·5–5·7) and 47 in the quarterly screening groups (6·7 per 1000 person-years; 4·8–8·6; table 3 and figure 2). Quarterly screening was associated with a significant increase in the detection rate of atrial fibrillation, compared with annual screening (HR 1·71; 95% CI 1·06–2·76; p=0·029). When only considering screen-detected atrial fibrillation (15 cases in the annual screening group and 28 cases in the quarterly screening group), quarterly screening was also associated with a significant increase in the detection rate of atrial fibrillation, compared with annual screening (HR 2·22; 95% CI 1·15–4·29; p=0·017). No significant interaction was observed for the detection of atrial fibrillation between screening groups and predefined subgroups defined according to age (65–74 years *vs* ≥75 years), sex, BMI (≤25 kg/m² *vs* >25 kg/m²), the presence of hypertension or diabetes, and a history of cardiovascular disease (figure 3). Analyses for diabetes and cardiovascular disease history were post hoc.

In further prespecified analyses, we compared the detection rate between the annual screening group and the two quarterly screening subgroups. 40 incident cases were detected in the quarterly screening group (7·2 per 1000 person-years; HR compared with annual screening, 1·83; 95% CI 1·12–3·00; p=0·02) and 7 incident cases in the quarterly screening plus group (4·8 per 1000 person-years; HR compared with annual screening 1·24; 0·54–2·86; p=0·61). There was no significant difference in detection rates between either quarterly screening groups (HR for the quarterly screening plus group compared with quarterly screening, 0·68; 0·30–1·52; p=0·35).

	Annual screening group (G1 [n=3244])	Quarterly screening group (G2)		p value
		Quarterly (G2·1 [n=2841])	Quarterly plus (G2·2 [n=721])	
Age, years	71·6 (6·3)	71·3 (6·1)	71·0 (6·2)	0·028
Sex, male	1410 (44%)	1259 (44%)	313 (43%)	0·78
Sex, female	1834 (56%)	1582 (56%)	408 (57%)	0·78
Body-mass index, kg/m²	24·5 (3·3)	24·6 (3·4)	24·5 (3·3)	0·16
Systolic blood pressure, mm Hg	137·7 (18·8)	137·5 (18·8)	137·5 (18·6)	0·89
Diastolic blood pressure, mm Hg	73·9 (9·5)	74·8 (9·5)	74·1 (9·5)	0·0022
Pulse rate, beats per min	73·6 (11·0)	73·4 (10·9)	72·8 (10·5)	0·15
Current smoking	468 (14%)	399 (14%)	92 (13%)	0·51
Alcohol intake	410 (13%)	360 (13%)	75 (10%)	0·22
Hypertension	1827 (56%)	1544 (54%)	421 (58%)	0·094
Diabetes	670 (21%)	576 (20%)	162 (23%)	0·43
History of cardiovascular disease				
Stroke or transient ischaemic attack	572 (18%)	501 (18%)	174 (19%)	0·82
Coronary heart disease	225 (7%)	189 (7%)	57 (8%)	0·50
Congestive heart failure	19 (1%)	12 (0%)	3 (0%)	0·63

Data are mean (SD) or n (%). Alcohol intake was defined as a per week volume of alcohol consumption of ≥5 g. Current smoking was defined as the present regular use of cigarettes (>1 per day) at the time of the study.

Table 1: **Baseline characteristics of the study participants**

	Annual screening group (G1 [n=3244])	Quarterly screening group (G2)		p value
		Quarterly (G2·1 [n=2841])	Quarterly plus (G2·2 [n=721])	
Number of scheduled follow-up visits	Two (once per year)	Eight (quarterly)	12 (eight quarterly + four once per week in the first month)	NA
Number of actual follow-up visits	1·6 (0·5)	3·5 (1·5)	5·2 (2·9)	<0·0001
Yearly visits				
Patients with one or more yearly visits	3244 (100%)	2680 (94%)	697 (97%)	<0·0001
Patients with two or more yearly visits	1855 (57%)	1534 (54%)	423 (59%)	0·014
Quarterly visits				
Patients with one or more quarterly visits	NA	2572 (91%)	633 (88%)	0·029
Patients with two or more quarterly visits	NA	2009 (71%)	477 (66%)	0·017
Patients with three or more quarterly visits	NA	1359 (48%)	336 (47%)	0·56
Patients with four or more quarterly visits	NA	681 (24%)	159 (22%)	0·30
Once per week visits				
Patients with one or more once per week visits	NA	NA	429 (60%)	NA
Patients with two or more once per week visits	NA	NA	362 (50%)	NA
Patients with three or more once per week visits	NA	NA	299 (42%)	NA
Patients with four once per week visits	NA	NA	204 (28%)	NA

Data are n (%) or mean (SD). p values are for the comparison between the three screening groups on yearly visits and between the quarterly and quarterly screening plus subgroups within the quarterly screening group. NA=not applicable.

Table 2: **Percentage of participants who completed a scheduled number of follow-up visits**

During follow-up, 130 participants died, including 35 deaths from cardiovascular cause. No significant between-group differences were observed for other clinical outcomes, including number of deaths, non-fatal ischaemic and haemorrhagic stroke, acute coronary syndrome, and uncontrolled hypertension (table 3).

We further compared the detection rate of annual, quarterly, and weekly ECG screenings. The incidence of newly diagnosed atrial fibrillation among participants that had two annual repeat screenings was 0·81% (15 of 1855). The yields of quarterly screenings during 2 years were 0·57% (three of 521) for one screen, 0·70% (four of 574) for two screens, and 1·94% (15 of 772) for three screens, whereas six or more quarterly screenings had the highest yield of 2·33% (eight of 344).

Of the 73 patients with incident atrial fibrillation during follow-up, 66 (90%) qualified for guideline recommended OAC prophylaxis. Of these 66 patients, 55 (83%) were followed up at the end of the study. Of these participants, 40 (73%) attended cardiovascular specialist clinics, 17 (43%) of whom were prescribed OAC (warfarin for eight patients, rivaroxaban for seven patients, and dabigatran for two patients). Two patients attended community health centres and were prescribed traditional Chinese medicine (n=1) and antiplatelet agents (n=1). 13 (24%) patients did not go to any doctor and did not take any antithrombotic drug. Of the 40 participants who attended cardiovascular specialist clinics, ten patients underwent either left atrial appendage occlusion (n=1) or catheter ablation (n=9), in which rivaroxaban was prescribed 3 months before and after procedure and was then discontinued.

Discussion

To our knowledge, our study is the first randomised clinical trial investigating the association between different screening frequencies of 30 s single-lead ECG and the detection rate of atrial fibrillation in a Chinese population. Our main finding was that quarterly ECG screenings showed a significantly higher detection rate than did annual ECG screenings; however, the addition of screenings once per week for the first month plus quarterly ECG screenings did not further increase the detection rate.

The total detection rate of atrial fibrillation, across screening groups, in the older (≥65 years) Chinese population in this study is similar to that observed in our previous study[21] done in 2011 (4·9 per 1000 person-years) and another community-based study done in Hong Kong.[22] A single timepoint 30 s ECG screening detected atrial fibrillation in 0·45% of the participants, whereas annual repeated ECG screenings in the first and second year detected atrial fibrillation in 0·81%, and three quarterly screenings further increased the detection rate to 1·94%. The highest detection rate was associated with six or more quarterly screenings, which had a yield of 2·3% in 2 years. These findings might support the notion that multiple ECG screenings with handheld single-lead ECG devices help to improve the detection rate. This notion was shown in the population screening of men and women, aged 75 and 76 years, for silent atrial fibrillation (STROKESTOP) study, in which the yield of new atrial fibrillation was 0·5% with the first screen and increased to 3·0% after 2 weeks of twice per day intermittent screening.[15] The remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation (REHEARSE-AF) study also identified a higher yield of 3·8% with the use of ECG recordings twice per week over 1 year, compared with screening in routine care.[16] The yield of atrial fibrillation detection in the quarterly screening group in our study is lower than that of the intervention groups in the STROKESTOP and REHEARSE-AF studies, which might be attributed to fewer ECG recordings in our study and the younger age of our study participants.

Quarterly plus once per week screenings was not associated with a further increase in the detection rate of atrial fibrillation. This result might be attributed to the small number of incident atrial fibrillation cases (n=7) in the quarterly screening plus subgroup. Nevertheless, it is also possible that the strategy of once per week screenings is not superior to the strategy of quarterly screenings. In

	Annual (G1) [n=3244]	Quarterly (G2)		G2 *vs* G1		G2·1 *vs* G1		G2·2 *vs* G1	
		Quarterly (G2·1 [n=2841])	Quarterly plus (G2·2 [n=721])	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
Primary outcome									
Incident atrial fibrillation	26 (4·1)	40 (7·2)	7 (4·8)	1·71 (1·06–2·76)	0·029	1·83 (1·12-2·99)	0·017	1·24 (0·54–2·86)	0·61
Other clinical outcomes									
Death from any cause	62 (9·9)	57 (10·3)	11 (7·6)	1·01 (0·71–1·43)	0·96	1·05 (0·73–1·51)	0·78	0·84 (0·45–1·56)	0·59
Death from cardiovascular cause	17 (2·7)	14 (2·5)	4 (2·8)	1·05 (0·54–2·04)	0·89	0·97 (0·47–1·99)	0·94	1·34 (0·49–3·65)	0·57
Ischaemic stroke	27 (4·3)	24 (4·3)	4 (2·8)	0·79 (0·46–1·34)	0·38	0·86 (0·49–1·50)	0·59	0·52 (0·18–1·49)	0·23
Haemorrhagic stroke	3 (0·5)	2 (0·4)	0	0·56 (0·09–3·35)	0·53	0·73 (0·12–4·39)	0·73	NA	NA
Acute coronary syndrome	32 (5·1)	30 (5·4)	7 (4·8)	0·90 (0·56–1·45)	0·67	0·93 (0·56–1·54)	0·78	0·80 (0·35–1·82)	0·59
Uncontrolled hypertension	764 (39·1%)	715 (39·3%)	210 (39·1%)	1·01 (0·89–1·14)	0·89	1·01 (0·89–1·15)	0·87	1·00 (0·82–1·22)	0·99

Data are number of events (per 1000 person-years), unless otherwise indicated. NA=not applicable.

***Table* 3: Primary outcome and other clinical outcomes**

the Danish LOOP study,[23] which evaluated the use of a large panel of screening strategies for atrial fibrillation detection with data from implantable loop recorders (Reveal LINQ, Medtronic, Minneapolis, MN, USA), detection was higher over the same monitoring duration when the periods between screenings were longer rather than shorter. The sensitivity of atrial fibrillation detection was 16·5% with once per week 24 h Holter monitoring for 3 weeks. It rose to 17·4% after 24 h Holter monitoring was done once per month for 3 months and to 19·5% when 24 h Holter monitoring was done annually for 3 years.[23] The diagnostic yield increased with the increase of the screening time interval.[23]

Screening studies have reported various rates of newly detected atrial fibrillation, depending on the method of screening and population risk factors.[15,16,24–27] Long-term continuous ECG monitoring with implantable loop recorders has detected more atrial fibrillation cases than all other strategies. Short episodes of atrial arrhythmia were found in approximately a third of patients across studies in which an implanted cardiac device or monitor was used for extended screening in individuals at high risk.[25–27] However, these recorders were not suitable for mass screening because of low cost-effectiveness. The Apple heart study[28] and the HUAWEI heart study[29] are good examples of atrial fibrillation screening with new wearable technology in adult populations, although the number of notifications of an irregular pulse was low.

The best approach to widespread screening in the general population might need to be individualised according to the requirements and resources of various countries and health-care systems. In our study, the percentage of patients who initiated OAC therapy during follow-up visits was low, being slightly more than 30%. There has been an improvement with education on the use of OAC therapy, compared with the survey data from community health centres,[30] which is similar to OAC therapy use in outpatients in tertiary hospitals.[31] Nonetheless, OAC therapy is still underused in patients with atrial fibrillation in China. The 80% of patients with atrial fibrillation taking OAC prescription in the HUAWEI heart study[28] might reflect a specific population who were much younger and probably had a higher health literacy and who chose to use smart wearable devices to monitor their own pulse rhythm. These people were probably more likely to seek and respond to a physician's advice and were

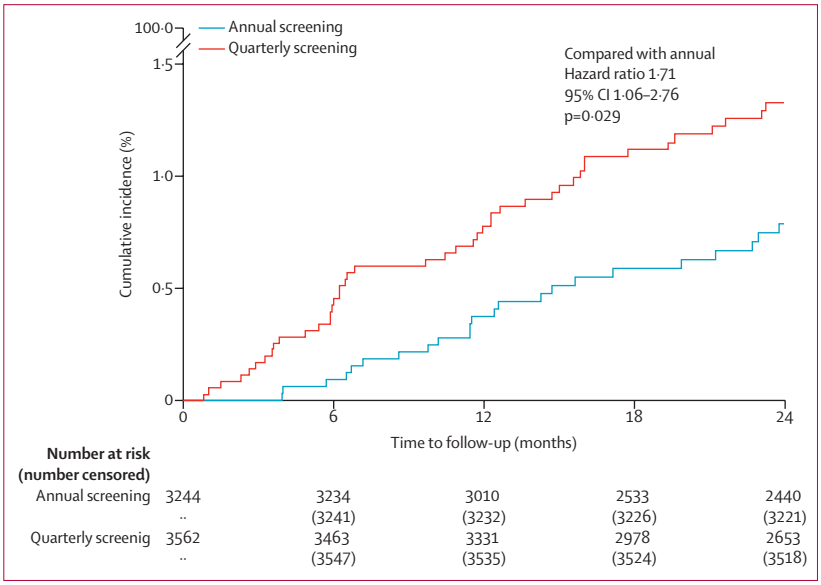

***Figure 2*: Cumulative incidence of atrial fibrillation according to the randomisation group**
Shown is the cumulative incidence of atrial fibrillation in the annual screening group and quarterly screening group with the use of a modified Kaplan-Meier approach.

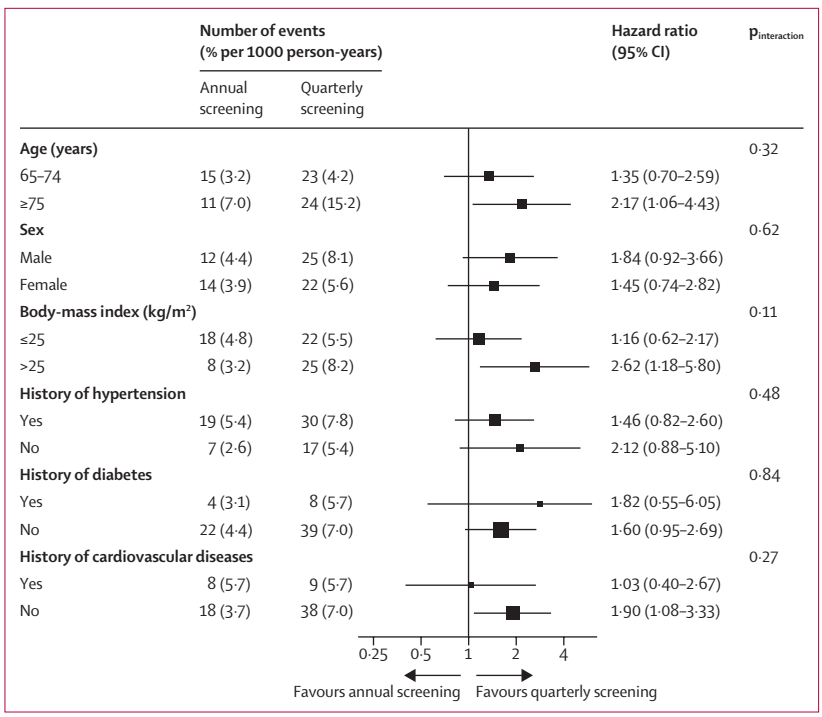

Figure 3: **Effects of quarterly versus annual screening on the detection of atrial fibrillation according to several baseline characteristics**

For subgroups, black squares represent point estimates, with the area of the square proportional to the number of events, and horizontal lines represent the 95% CI.

more likely able to pay for the non-vitamin K OAC medications. Therefore, the HUAWEI heart study[32] reported a 4·1% absolute reduction in the primary endpoints of ischaemic stroke, systemic thromboembolism, death, and rehospitalisation in their intervention group. Conversely, we observed no significant between-group differences for hard clinical outcomes such as stroke or mortality. A key point might be the poor downstream management after a new diagnosis of atrial fibrillation via screening; without an appropriate anticoagulation prescription to those with new atrial fibrillation, no benefit in stroke reduction will accrue.

In this context, even though quarterly screening in Chinese participants was feasible and more effective than was annual screening in Shanghai, effort should be made to increase the use of OAC treatment in known atrial fibrillation before more frequent or intensive screening for atrial fibrillation could be recommended in China. Atrial fibrillation disease education and advice on specialist referral implemented in our study were still insufficient to close the treatment gap. More effective downstream management pathways and health resource allocations are required to overcome these barriers. Directed heath resource allocations for patients to access anticoagulant drugs and international normalised ratio testing in community health centres, such as a regular specialist outreach clinic, might help to enhance adherence and long-term persistence with OAC.

Our study should be interpreted within the context of some limitations. First, adherence to protocol was low, partly because the once per week and quarterly scheduled follow-up visits at community health centres were not as convenient as patient-activated self-monitoring at home. Second, most of the participants in one community health centre (Yuyuan Community Health Centre) dropped out because they moved to distant communities because of the housing demolition and relocation ongoing in Shanghai. It is also possible that patients who were more unwell had a greater dropout rate. However, this possibility was not supported by a search of death records and yearly examination records, which showed no differences in those who adhered to schedule and those who did not in the five community health centres. Third, the detection rate of atrial fibrillation was low, which might be related to the low adherence to screening schedule as mentioned earlier. The detection rate of atrial fibrillation for quarterly screening might be better if there were a higher adherence to screening. Involving physicians from the community health centres in the screening programme in future studies might encourage adherence and improve the detection rate. Although the detection rate appears to be low, this would equate to 1 million more people per year in China being diagnosed with atrial fibrillation if quarterly screening was routine, and potentially approximately 50 000 strokes prevented each year. Finally, despite offering atrial fibrillation disease education and advice on specialist referral, the use of OACs in patients with newly diagnosed atrial fibrillation was low, which calls for more effective downstream management pathways and health resource allocations in the future.

In conclusion, quarterly 30 s single-lead ECG screening significantly increased the detection rate of atrial fibrillation compared with annual ECG screening in older Chinese individuals, but additional once per week screening in the first month did not increase the yield of new atrial fibrillation. Our study contributed data on atrial fibrillation screening in a population at high risk aged 65 years and older, living in a developed urban area of China. Whether this more intensive screening strategy could be widely recommended requires further investigation across a larger geographical area and larger population.

Contributors

J-GW and BF designed and supervised the study. WZ, YC, and C-YM coordinated the study and data collection. DW, Q-FH, C-SS, and YL participated in the recruitment of patients and data management. SS, S-KX, LL, DZ, Y-LC, L-XH, J-HX, Y-BC, YW, and Q-HG participated in the follow-up of the study participants. WZ and YC, together with J-GW and NL, did the statistical analyses, interpreted the data, and prepared the first draft of the manuscript. X-FY was responsible for randomisation in the recruitment of patients. All authors were involved in data interpretation, reviewed and revised the manuscript, and approved the final version for submission. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. WZ and YC, together with J-GW, accessed and verified the data.

Declaration of interests

J-GW reports receiving lecture and consulting fees from Novartis, Omron, and Takeda; and grants from Bayer. BF reports grants from

Bayer Healthcare Company and BMS-Pfizer; personal fees from Bayer Healthcare Company, BMS-Pfizer, Daiichi-Sankyo, and Omron; and non-financial support from Bayer, BMS-Pfizer, Daiichi-Sankyo, and Omron. All other authors declare no competing interests.

Data sharing

Data cannot be shared publicly because of ethical restrictions. Data are available from Ruijin Hospital Ethics Committee (contact via wyfkjc@163.com) for researchers who meet the criteria for access to confidential data.

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