Mass Screening for Untreated Atrial Fibrillation
The STROKESTOP Study

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Background—The aims of the present study were to define the prevalence of untreated atrial fibrillation (AF) in a systematic screening program using intermittent ECG recordings among 75- to 76-year-old individuals and to study the feasibility of initiating protective oral anticoagulant (OAC) treatment.

Methods and Results—Half of the 75- to 76-year-old population in 2 Swedish regions were invited to a screening program for AF. Participants without a previous diagnosis of AF underwent intermittent ECG recordings over 2 weeks. If AF was detected, participants were offered OAC. During the 28-month inclusion period, 13 331 inhabitants were invited. Of these, 7173 (53.8%) participated. Of the participants, 218 (3.0%; 95% confidence interval [CI], 2.7–3.5) were found to have previously unknown AF, and of these, AF was found in 37 (0.5% of the screened population) on their first ECG. The use of intermittent ECGs increased new AF detection 4-fold. A previous diagnosis of AF was known in 9.3% (n=666; 95% CI, 8.6–10.0). Total AF prevalence in the screened population was 12.3%. Of participants with known AF, 149 (2.1%; 95% CI, 1.8–2.4) had no OAC treatment. In total, 5.1% (95% CI, 4.6–5.7) of the screened population had untreated AF; screening resulted in initiation of OAC treatment in 3.7% (95% CI, 3.3–4.2) of the screened population. More than 90% of the participants with previously undiagnosed AF accepted initiation of OAC treatment.

Conclusions—Mass screening for AF in a 75- to 76-year-old population identifies a significant proportion of participants with untreated AF. Initiation of stroke prophylactic treatment was highly successful in individuals with newly diagnosed AF.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01593553.

Key Words: anticoagulants ■ atrial fibrillation ■ mass screening ■ prevention and control ■ stroke

The prevalence of atrial fibrillation (AF) has been estimated to be >3% in the adult population.1 AF can be asymptomatic and intermittent, making diagnosis difficult. Camm et al2 have suggested that asymptomatic AF represents a third of the total AF population, a result confirmed in pacemaker studies.3

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The most feared complication in AF patients is ischemic stroke, a risk independent of the nature of AF.1–4 Instead, risk factor assessment (CHA2DS2-VASc score) is used to identify individuals with AF who are at risk of ischemic stroke.5 The CHA2DS2-VASc score takes into account congestive heart failure, hypertension, age, diabetes mellitus, previous stroke/transient ischemic attack (TIA), vascular disease, and female sex. At ≥75 years of age, current guidelines from the European Society of Cardiology recommend oral anticoagulant (OAC) treatment for AF regardless of other risk factors.5 OAC treatment reduces the risk of ischemic stroke by 64% to 70%,7,8 but undertreatment remains a significant clinical problem.9,10

In the latest European Society of Cardiology guidelines, opportunistic screening for AF is recommended.7

The STROKESTOP study is an ongoing study to determine whether systematic screening for untreated AF and initiation of OAC treatment can reduce the risk of ischemic stroke cost-efficiently over 5 years of follow-up.

The aim of this first report from the STROKESTOP study is to present baseline results on the prevalence of new and known AF from intermittent systematic ECG screening and the feasibility of initiating OAC treatment.

Methods

Study Population
The study design was described in a previous publication.11 Individuals born in 1936 to 1937 living in Stockholm County (n=23
888) or in the Halland region (n=4880) at the end of 2011 were identified by their unique civic registration numbers. A computerized 1:1 randomization was performed in the 75- to 76-year-old population with stratification for sex, year of birth, and region. If the individual was randomized to the screening arm, an invitation to participate in an AF screening program was sent by mail. Nonresponders received 1 reminder in Halland and 2 reminders in Stockholm. Individuals who died before or during the invitation process were identified and excluded (Figure 1). Information on nationality at birth was obtained from the Swedish Central Bureau of Statistics.

Screening Procedure
Participants were informed orally and in writing at a screening center and signed informed consent forms before entering the study. Medical history, including AF, stroke/TIA, heart failure, hypertension, diabetes mellitus, myocardial infarction, or vascular disease, was obtained, as well as whether participants were on OAC or antiplatelet therapy. In Stockholm, participants also self-assessed height and weight. Participants without a previous history of AF who were in sinus rhythm on the first visit were instructed in the use of a handheld ECG recorder for intermittent ECG recordings over 2 weeks. An index ECG for detection of permanent arrhythmia was obtained. A 1-lead ECG recorder from Zenicor (www.zenicor.com) with an integrated mobile transmitter that sends 30-second ECG strip data to a data-base was used. Participants placed their thumbs on the device twice daily and whenever they noticed palpitations. The device has been shown to have higher sensitivity for detection of AF than conventional 24-hour Holter recordings.12–14 In cases of inconclusive ECG tracings, participants were offered additional ECG recordings according to the investigating cardiologist’s judgment.

Definition of AF
AF was defined as at least one 30-second recording with irregular rhythm without p waves15 or a minimum of 2 similar episodes lasting 10 to 29 seconds during 2 weeks of intermittent recording. Research nurses, whose ECG skills were verified by random controls, manually assessed all ECG recordings. All abnormal ECGs were referred to the investigating cardiologist. If there was uncertainty about the presence of AF, the ECGs were adjudicated by a consensus group. In patients in whom other significant arrhythmias were detected, referral was made as appropriate.

Patients With Detected AF
All individuals with new AF and AF patients without OAC treatment were offered structured follow-up by a cardiologist to ensure adequate treatment, following current European guidelines.7

Statistical Methods
Continuous variables are reported as mean±SD. For continuous variables, the Student t test was used. For proportions, the Fisher exact test or χ² tests were used. Ordinal data were analyzed with the Mann-Whitney U or Kruskal-Wallis test. Two-tailed tests were applied. A multivariable analysis was performed with logistic regression. The discriminative ability of the model was estimated as c statistics. A value of P<0.05 was regarded as significant. These analyses were performed with IBM SPSS statistics version 22 software (IBM SPSS Statistics, IBM Corp, Somers, NY) and Open-Epi (Open Source Epidemiological Statistics for Public Health) version 3.01.

Ethics
The study complies with the Declaration of Helsinki, and the protocol was approved by the regional ethics committee (DNR 2011-1363/31/3). Informed consent was obtained from all participants in the screening program (http://www.clinicaltrials.gov; identifier, NCT01593553).

Results
Participation
Screening started in March 2012 and concluded in June 2014. In total, 14387 inhabitants were invited to take part in screening. Before the invitation process was completed, 1056 individuals died. The remaining individuals’ response was 54% (7173 participants), which increased with additional invitations (Figure I in the online-only Data Supplement).

The participants registered 189715 ECG recordings, with an average of 26.4 per subject. Only 1% made <15 ECG recordings. Because of difficulties in diagnosing AF from the recordings, 3.5% of participants were referred for 24-hour monitoring. Two patients withdrew their consent to participate. Referral for further workup was made in 10 patients as a result of high-grade atrioventricular block or sick sinus syndrome. Only 2% of participants (n=144) were of non-European descent.

Characteristics for participants are shown in Table 1.

Prevalence of AF
New AF was detected in 218 patients (3.0%; 95% confidence interval [CI], 2.7–3.5). A previous diagnosis of AF was present in 666 patients (9.3%; 95% CI, 8.6–10.0), the majority of whom were men (n=407, 61.6%). Among those with known AF, 517 of 666 (77.6%) were using OACs at the index visit. Thus, 149 patients with known AF were not using OACs, constituting 2.1% (95% CI, 1.8–2.4) of the screened population. Hence the prevalence of untreated AF was 5.1% (95% CI, 4.6–5.7).

In participants who received a new diagnosis of AF, the mean number of registrations with AF was 4.5 (95% CI, 3.4–5.6). In 40 individuals, the diagnosis was made from 1 single pathological registration during intermittent screening (Figure 2). In 12 individuals, AF was diagnosed from ≥2 episodes ranging from 10 to 29 seconds.

Most participants with new AF were diagnosed during the first days of their 2-week ECG registration period (Figure 3).
Only 37 cases were diagnosed from the ECG at the index visit. Intermittent monitoring diagnosed 4 times as many individuals with new AF compared with the index ECG (Figure II in the online-only Data Supplement).

Atrial flutter was diagnosed in 8 patients, and they were included in the AF group.

The total number of AF cases in the screened population was 884 (12.3%). Intermittent screening revealed 33% more cases of AF than previously known.

**Use of OACs**

Men with known AF were treated with OACs more often (80.8% versus 72.4%; \(P<0.05\)). In summary, 5.1% (95% CI, 4.6–5.7) of the participants in screening had AF and were

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**Table 1. Baseline Characteristics at Study Entry**

<table>
<thead>
<tr>
<th></th>
<th>Known AF (n=666)</th>
<th>New AF (n=218)</th>
<th>No AF (n=6289)</th>
<th>(P) Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>124 (19.5)</td>
<td>6 (2.8)</td>
<td>117 (1.9)</td>
<td>0.307</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>389 (59.4)</td>
<td>113 (52.1)</td>
<td>3064 (48.9)</td>
<td>0.370</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>135 (20.3)</td>
<td>29 (13.3)</td>
<td>630 (10.0)</td>
<td>0.136</td>
</tr>
<tr>
<td>Previous stroke/TIA, n (%)</td>
<td>137 (20.7)</td>
<td>21 (9.6)</td>
<td>490 (7.9)</td>
<td>0.309</td>
</tr>
<tr>
<td>Vascular disease, n (%)</td>
<td>115 (17.5)</td>
<td>31 (14.3)</td>
<td>518 (8.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>254 (38.4)</td>
<td>99 (45.4)</td>
<td>3496 (55.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>CHA2DS2-VASc score, mean±SD</td>
<td>3.9±1.5</td>
<td>3.5±1.2</td>
<td>3.4±1.0</td>
<td>0.392</td>
</tr>
<tr>
<td>CHA2DS2-VASc score, median (IQR)</td>
<td>4 (2)</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>0.42</td>
</tr>
<tr>
<td>OAC treatment, n (%)</td>
<td>517 (77.6)</td>
<td>5 (2.3)</td>
<td>99 (1.6)</td>
<td>0.26</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>122 (18.3)</td>
<td>54 (24.8)</td>
<td>1452 (23.1)</td>
<td>0.57</td>
</tr>
<tr>
<td>Height, mean (SD; n=5179), cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>173.8 (8.9)</td>
<td>172.9 (8.4)</td>
<td>170.0 (9.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td>165.7 (6.4)</td>
<td>165.3 (5.6)</td>
<td>163.7 (6.6)</td>
<td>0.054</td>
</tr>
<tr>
<td>Men</td>
<td>178.7 (6.4)</td>
<td>178.0 (6.3)</td>
<td>177.2 (6.6)</td>
<td>0.27</td>
</tr>
<tr>
<td>Weight (n=4907), kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>81.6 (17.0)</td>
<td>81.4 (18.0)</td>
<td>74.7 (14.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women</td>
<td>72.3 (13.5)</td>
<td>79.7 (23.3)</td>
<td>68.9 (13.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Men</td>
<td>86.9 (16.7)</td>
<td>82.5 (13.6)</td>
<td>81.3 (12.1)</td>
<td>0.37</td>
</tr>
<tr>
<td>BMI (n=4837), kg/m²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>26.9 (4.8)</td>
<td>27.3 (6.6)</td>
<td>25.8 (5.5)</td>
<td>0.012</td>
</tr>
<tr>
<td>Women</td>
<td>26.5 (4.8)</td>
<td>29.3 (8.2)</td>
<td>25.8 (6.8)</td>
<td>0.010</td>
</tr>
<tr>
<td>Men</td>
<td>27.2 (4.8)</td>
<td>26.1 (3.9)</td>
<td>25.9 (3.5)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; BMI, body mass index; IQR, interquartile range; OAC, oral anticoagulant; and TIA, transient ischemic attack.

*Comparisons done between Newly diagnosed AF and NO AF.
without OAC protection. Men (n=367) constituted 53.7% of the untreated population.

**Initiation of OACs**

In participants with new AF, 93% accepted starting OAC treatment. The main reason for not initiating OAC treatment in participants with new AF was patient preference (see Figure 4).

In participants with known but untreated AF, anticoagulant treatment was initiated in 70 of 149 (47%). The main reason for not initiating OAC treatment was patient preference. Contraindications to OAC treatment were found in 14% of individuals in this group. Of 128 participants without contraindications, OAC treatment was started in 70 (55%).

Initiation of OAC treatment was made in 3.7% (95% CI, 3.3–4.2) of the screened population. The choice of which OAC to be prescribed was made according to the patients’ preferences. New OACs were initiated in 73%.

**Risk Factors: Prediction of AF**

Participants with known vascular disease were more likely to be diagnosed with AF, and women were less likely to receive a new diagnosis of AF (Table 1 and Figure III in the online-only Data Supplement).

Participants with new AF were in general significantly taller and heavier with a higher body mass index compared with participants without AF. Mean CHA2DS2-VASc score did not differ significantly between the newly diagnosed AF group and participants free of AF. However, there was a significant (P<0.001) association between increasing CHA2DS2-VASc score and prevalence of AF (Figure 5). Participants with known AF had higher CHA2DS2-VASc scores (mean, 3.94; median, 4) than participants with newly detected AF (mean, 3.47; median, 3; P<0.001) and participants without AF (mean, 3.40; median, 3; P<0.001).

A multivariable analysis showed that the strongest predictor for AF (new or known) in the screened population was congestive heart failure, followed by previous stroke/TIA, diabetes mellitus, height (odd ratio per 1-cm increase), and weight (odds ratio per 1-kg increase; see Table 2).

Previous studies16,17 have used risk scores to predict the development of AF. We calculated a modified score on the basis of the work of the Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation (CHARGE-AF)16 Consortium, using height, weight, history of diabetes mellitus, hypertension, vascular disease, and congestive heart failure, which showed a modest capacity to predict in which patients AF was most likely (c statistic, 0.692; 95% CI, 0.670–0.717).

To study whether any group would not benefit from screening, a multivariable analysis was performed to compare risk factors for participants in whom AF was detected compared with the group with no detection of AF (Table I in the online-only Data Supplement). Female sex, lower weight, and absence of vascular disease were significantly associated with no detection of AF. In women with a body mass index <25 kg/m², screening yielded only 1.3% new AF.

**Regional Differences**

Participation in the screening program was higher in rural Halland than in urban Stockholm (64% versus 52%; P<0.001), and AF was a more commonly found in Halland (4.0% versus 2.8%; P=0.02). In Halland, individuals with known AF were more likely to be on OACs (87% versus 75%; P=0.001; Table II in the online-only Data Supplement).

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**Figure 4.** Initiation of oral anticoagulant (OAC) treatment. AF indicates atrial fibrillation; F/U, follow-up; GI, gastrointestinal; and ICH, intracranial hemorrhage.
Discussion
This is the first multicenter, prospective, population-based systematic AF screening study using intermittent ambulatory ECG recordings to screen for not only permanent but also paroxysmal AF. This is also the first study reporting the yield after AF screening in terms of initiation of OAC treatment and the first study with plans for long-term follow-up and a thorough study of health economy. New AF was found in 3.0% (95% CI, 2.7–3.5) of the screened population, whereas only 0.5% were found on the first ECG. Intermittent ECG screening increased the prevalence of AF in the screened population by 33%. Of the participants 2.1% (95% CI, 1.8–2.4) had known AF but no OAC treatment.

Thus, our study revealed that 5.1% of the screened population had untreated AF. More than 90% of patients with newly diagnosed AF accepted initiation of OAC treatment. Preventive OAC treatment because of untreated AF was initiated in 3.7% of the screened population.

Inclusion and Uptake
Compared with established screening programs in Sweden, participation was lower.18–20 However, participation in epidemiological studies has shown a declining trend,21 and compared with participation in another large research study in Sweden, our participation was higher.22 Factors that could explain a lower participation include the fact that the general public could perceive that partaking in a research screening program over 14 days is more cumbersome than participating in a single-visit established screening program. In addition, the age selected for our study was higher than in other programs; higher age is associated with more disability, which could affect participation.23 The invitation was written in Swedish, which could exclude non–Swedish-speaking participants.

Prevalence and Prediction of AF
Previous screening studies for AF have focused on strategies using screening for AF at a single time point, which is likely to detect only permanent arrhythmia and might miss most patients with paroxysmal arrhythmia. Intermittent ECG recording has shown a higher detection rate of AF compared with 24-hour Holter monitoring.13 In a meta-analysis of screening programs, using a single ECG recording found new AF in 1.4% of subjects >65 years of age.24 The current recommendation in the European Society of Cardiology guidelines for opportunistic screening for AF is based on a study comparing opportunistic ECG screening using pulse palpation in which the investigators found 1.64% new AF with systematic screening using 12-lead ECGs and 1.62% new AF was found in a population with a mean age of 75 years.7,23 Our study found 0.5% new AF via the initial ECG recording (Figure II in the online-only Data Supplement), but with intermittent systematic screening, detection of new AF increased 4-fold to 3%

![Figure 5. Association between CHA2DS2-VASc score and prevalence of atrial fibrillation (P<0.001, Kruskal-Wallis test).](image)
of the screened population, which is almost double the prevalence of previous studies in which single-time-point ECG screening was performed.23,24 This might indicate that AF is well recognized and treated in Sweden and that most individuals with a more permanent arrhythmia have already been diagnosed. The use of an intermittent ECG recorder is more likely to detect patients earlier before AF becomes permanent.15

Before intermittent ECG screening, the screened population reported a 9.3% prevalence of AF. This is a higher prevalence of AF compared with studies of populations of similar age groups in North America,25-26 the UK,27 and Greece28 and slightly lower than Icelandic and Dutch prevalence studies.29,30 Systematic screening for AF in populations of a similar ethnicity in which the prevalence of known AF is lower would likely yield a higher rate of newly discovered AF, which would further increase the cost-effectiveness of systematic AF screening. The majority of AF prevalence studies have been performed in Western European countries and in North America. Studies from low- and middle-income countries indicate a lower AF prevalence,31 but as the population ages and the prevalence of risk factors for AF increases, AF prevalence is likely to increase in these areas,32 and systematic AF screening might become beneficial.

Our multivariable analysis showed that the strongest predictor for AF (new or known) in the screened population was heart failure, previous stroke/TIA, and diabetes mellitus. Our results are consistent with results from the Framingham study in which congestive heart failure was also shown to be one of the most important risk factors for AF with a 4.5- and 5.9-fold increased risk in men and women, respectively, whereas diabetes mellitus conferred a risk of 1.4 and 1.6, respectively.33 A history of stroke/TIA was also a predictor for AF. According to current European stroke guidelines,34 these patients should already have been screened for AF with 24-hour Holter monitoring unless another cause for stroke was apparent. This short monitoring period, which differs from the more extended screening for AF in the American Heart Association guidelines,35 presumably leads to under-detection of AF.36

Individuals with vascular disease were diagnosed with new AF to a greater extent, despite the fact that they most likely had already been subjected to cardiovascular workup (increasing the probability that AF should have been diagnosed). This could signify that individuals with vascular disease are more prone to developing AF37 but also shows what a difficult end point AF is because of its asymptomatic and intermittent nature. Participants who weighed more, were taller, and had a higher body mass index were more likely to receive a diagnosis with AF, which is in accordance with previous studies.38,39

In women with a body mass index <25 kg/m², only 1.3% new AF was found. This might indicate that in women AF screening might be initiated at an older age because the prevalence of AF is lower in women compared with men in the same age category.9 However, women have a higher risk of stroke compared with men,39 so continuing screening at the same age as men might still be pertinent because the individuals found are at a higher risk.

Participants with known AF had more comorbidity. Increasing CHA2DS2-VASc scores correlate with an increased presence of AF (Figure 5).

In a pilot study, individuals 75 years of age with at least 1 additional risk factor for stroke underwent screening for silent AF with intermittent ECG registration.40 Previously untreated AF was found in 7% of the participants. In the pilot study, patients with newly diagnosed AF had a CHA2DS2-VASc mean score of 3.85 and a median score of 4; in the present study, the respective scores were 3.47 and 3. This difference (P=0.03) in comorbidity may explain some of the difference in AF prevalence.40

Initiation of OAC Treatment

In patients with new AF, acceptance of treatment with OACs despite a lack of symptoms was high. A possible reason is that a cardiologist with special interest in AF did the workup. More than 70% of participants chose treatment with novel OACs. Compared with previous studies,34,41,42 a greater proportion of participants with known AF were on OAC treatment than expected. The invitation stated that patients with AF would be referred for OAC treatment; hence, patients with a negative attitude toward OACs might have chosen not to participate. Individuals attending screening might be more health aware and therefore on correct treatment. Initiation of OAC treatment in participants with known AF was lower compared with those with new AF. The same cardiologists initiated treatment for both groups, so patient information was similar. There could be several reasons for lower initiation. Individuals with known AF could have tried and discontinued OAC treatment, making them less willing to try again. There could be difficulties in realizing the risks of untreated AF, especially in patients who avoided long-term treatment without suffering consequences or received erroneous information in the past that aspirin would suffice. In this study, almost 20% of individuals with known AF were treated with aspirin despite poor effects on stroke prevention in individuals with AF.43 In an AF population less well treated with OAC, it is probable that systematic screening could yield further increases in OAC treatment among participants.

Regional Differences

In Halland, screening uptake was greater, which could be explained in part by decentralized organization of screening compared with the centralized organization in Stockholm. Differences in screening uptake within each area might also be correlated to socioeconomic status.44 Proportionally more cases of new AF were found in Halland compared with Stockholm (4.0% versus 2.8%). Screening uptake is usually poorer among individuals who are more prone to have the condition being investigated.45 The regional difference in participation might explain the difference in detection of new AF if AF prevalence is higher in the group not attending in Stockholm.

Cost-Effectiveness

The Swedish central government agency of Dental and Pharmaceutical Benefits, TLV, has the role of determining whether a pharmaceutical product shall be subsidized by the
state and has recently published an extensive analysis on the cost-effectiveness of screening for AF with intermittent ECG recordings. It predicts that the STROKESTOP screening program would incur a cost of €4164 per quality-adjusted life-year when a lifelong perspective is used, which is regarded as a low cost per quality-adjusted life-year. It could hence be implied that, in a 75- to 76-year-old population of similar ethnicity, screening for AF will be cost-effective.

Screening for AF Compared With Other Screening Programs
The World Health Organization lists 10 conditions (Table III in the online-only Data Supplement) that should be fulfilled to justify mass screening. AF meets all of these criteria. In screening for malignancies, conditions that might not affect the patients’ life expectancy or symptoms might be found. In contrast, in screening for AF, there is an instantaneous indication for initiating OAC treatment in individuals at risk of thromboembolic events.

Several other screening programs have already been implemented and have been accepted by society. The diagnostic yield of these programs is lower than that of screening for AF.

Limitations
Because the registration period was limited to 14 days and the participants were monitored only <1% of the time, there was probably underdetection of AF. A patient who has AF detected in this brief period of monitoring is presumably one with a high burden of AF. It is plausible that continuous monitoring with an implantable device would increase the yield of AF, but the upfront costs would be greater, and the procedure probably would be less acceptable to the participants.

Atrial flutter can remain undiagnosed because its detection can be difficult with this method. Because atrial flutter is an arrhythmia more commonly observed in blacks compared with other racial groups, this might be more of a concern in black populations. These limitations should be weighed against the ease of use and high degree of compliance.

Most clinicians unfailingly agree to initiate OAC treatment in individuals with asymptomatic AF and increased CHADS2-VASc score if AF is found on passant on a regular health check, and a recent study of stroke risk in incidentally discovered AF supports this. However, the relationship between AF burden and stroke risk is not fully established. In 28.6% of individuals with AF detected by intermittent ECGs, the diagnosis was made from 1 episode of AF, and 12 individuals presented with ≥2 episodes of AF <30 seconds, likely representing a low AF burden. In studies using continuous monitoring such as the Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT), no clear temporal relationship between duration of AF and stroke has been seen. In a recent study of patients with implanted cardiac devices, a threshold of ≥5 minutes during a median monitoring period of 24 months was statistically significantly associated with the occurrence of ischemic stroke. However, AF of a duration <5 minutes was not studied. Compared with continuous monitoring, the finding of AF on intermittent monitoring is likely to signify a high AF burden because the monitoring represents a short temporal time frame.

Self-reporting of risk factors could lead to partially erroneous reporting of comorbidity, but in our pilot study, patient information on (self-reported) comorbidity was accurate in 99% of cases.

Studies comparing AF prevalence across different racial groups have shown heterogeneity with a higher prevalence in whites compared with blacks, Hispanics, and Asians. This difference remains even if AF prevalence is studied in pacemaker studies, in which differences in healthcare consumption patterns are of no importance. Even though AF was less common in blacks compared with whites in a study of an American biracial population, stroke remained a vast problem, with higher incidence rates than in the white population, raising the possibility that the importance of AF as a risk factor for stroke might vary between ethnic groups.

Our data describe a population in which 98% of participants were of European descent. Hence, systematic screening for AF in a population with different racial composition might yield a lower prevalence.

The questions of whether screening for AF and initiating OAC treatment will reduce the risk of ischemic stroke and to what extent individuals are compliant with treatment remains to be investigated. We plan to follow up on our participants in 5 years using data from the national health registries and the national prescription registries to observe whether intermittent screening for AF and initiating OAC treatment will reduce the risk of stroke compared with the nonscreened population.

Conclusions
Mass screening in 75- to 76-year-old individuals with intermittent ECG recordings yields a considerable proportion of individuals with untreated AF who can be started on OAC treatment.

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References


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**CLINICAL PERSPECTIVE**

Stroke is the second leading cause of death worldwide. Atrial fibrillation (AF), already the most common sustained cardiac arrhythmia with a prevalence of 1.5% to 2% of the adult European population, is expected to double in prevalence by 2050 as a result of an aging population. AF increases the risk of ischemic stroke 5-fold, even though a large proportion of patients with AF remain completely asymptomatic. In addition, AF can be difficult to diagnose because of its intermittent nature. If an AF diagnosis is made, the risk of stroke can be reduced by up to 70% by oral anticoagulant treatment. However, oral anticoagulant undertreatment is common. For this mass screening trial, STROKESTOP, >13,000 Swedish inhabitants 75 to 76 years of age were invited to participate in a systematic screening program for AF. More than 50% chose to participate in the screening program, which used intermittent 2-week ECG recordings to diagnose AF. With the intermittent screening, the prevalence of known AF in the screened population increased by >30%, from 9 to 12%. All participants with untreated AF, who constituted 5.1% of the screened population, were referred for oral anticoagulant treatment, and 3.7% accepted initiation of treatment.
Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study
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## Supplemental Material

### Supplemental Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimated ( \beta ) (SE)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure (Yes)</td>
<td>-0.136 (0.434)</td>
<td>0.87 (0.37-2.04)</td>
<td>0.750</td>
</tr>
<tr>
<td>Hypertension (Yes)</td>
<td>-0.074 (0.141)</td>
<td>0.93 (0.7-1.22)</td>
<td>0.600</td>
</tr>
<tr>
<td>Diabetes Mellitus (Yes)</td>
<td>-0.194 (0.209)</td>
<td>0.82 (0.55-1.24)</td>
<td>0.350</td>
</tr>
<tr>
<td>Prior stroke/TIA (Yes)</td>
<td>-0.138 (0.237)</td>
<td>0.87 (0.55-1.39)</td>
<td>0.560</td>
</tr>
<tr>
<td>Vascular disease (Yes)</td>
<td>-0.48 (0.207)</td>
<td>0.62 (0.41-0.93)</td>
<td>0.020</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>0.358 (0.14)</td>
<td>1.43 (1.09-1.88)</td>
<td>0.010</td>
</tr>
<tr>
<td>Height, cm</td>
<td>-0.007 (0.015)</td>
<td>0.99 (0.96-1.02)</td>
<td>0.620</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>-0.021 (0.006)</td>
<td>0.98 (0.97-0.99)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Supplemental Table 1 – Factors associated with lack of detection of AF using intermittent ECG recordings: Multivariable Analysis. Odds ratio calculated for height calculated per 1 cm increase and weight per 1 kg increase

AF= Atrial Fibrillation. TIA= transient ischaemic attack
## Supplemental Table 2 Demographics

<table>
<thead>
<tr>
<th></th>
<th>Stockholm</th>
<th>Halland</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population density (individuals/km²)</td>
<td>329</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Life expectancy (years)</td>
<td>83.1(female)/78.7(men)*</td>
<td>83.8(female)/79.7 (men)*</td>
<td></td>
</tr>
<tr>
<td>Physician per inhabitants</td>
<td>446/100 000†</td>
<td>293/100 000†</td>
<td></td>
</tr>
<tr>
<td>Prevalence AF from registry studies ‡</td>
<td>9.2%</td>
<td>9.4%</td>
<td></td>
</tr>
<tr>
<td>Mode of screening (No screening centras)</td>
<td>Central (1)</td>
<td>Local (6)</td>
<td></td>
</tr>
<tr>
<td>Number of invites</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Participation. %</td>
<td>5672 (52%)</td>
<td>1501 (64%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Newly diagnosed AF</td>
<td>158 (2.8%)</td>
<td>60 (4.0%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Previously known AF</td>
<td>523 (9.2%)</td>
<td>143 (9.5%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Previously known AF w/o OAC (% of all known AF)</td>
<td>131 (25.0%)</td>
<td>18 (12.6%)</td>
<td>0.0014</td>
</tr>
<tr>
<td>Total AF prevalence</td>
<td>12.0%</td>
<td>13.5%</td>
<td>0.11</td>
</tr>
<tr>
<td>CHA2DS2-VASc mean (all)</td>
<td>3.45</td>
<td>3.46</td>
<td>0.91</td>
</tr>
<tr>
<td>Chads-Vasc median (all)</td>
<td>3</td>
<td>3</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*Demographic data were collected from Statistics Sweden
† Data from Social Board of Health and Welfare Sweden
‡ Personal data courtesy of Leif Friberg
Supplemental Table 3
Wilson–Jungner criteria for appraising the validity of a screening program endorsed by the World Health Organization. 1968

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease
3. Facilities for diagnosis and treatment should be available
4. There should be a recognizable latent or early symptomatic stage
5. There should a suitable test or examination
6. The test should be acceptable to the population
7. The natural history of the condition including development from latent to declared disease. should be adequately understood
8. There should be an agreed policy on whom to treat as patients
9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
10. Case finding should be a continuing process and not a ‘once and for all’ project
Supplemental Figure 1

Cumulative attendance per invitation. In Halland only two invites were issued.
Supplemental Figure 2
Mode of AF detection

New AF
n=218

Intermittent ECG
n=177

Holter/other ECG
n=41

Index ECG
n=37

Intermittent ECG
N=140
Supplemental Figure 3

Clinical Characteristics in participants with newly diagnosed AF compared to no AF. CHF= congestive heart failure. TIA=transient ischaemic attack.
고령자에 대한 대규모 선별검사로 심방세동 치료의 소외 대상자를 줄일 수 있다: STROKESTOP 연구

오 세일 교수 서울대학교병원 순환기내과

초록

배경

본 연구의 목적은 75-76세 연령층에서의 간헐적인 심전도 모니터링을 이용한 체계적 선별검사 프로그램을 통해 치료받지 않은 심방세동의 유병률을 확인하고 예방적인 경구용 항응고제 치료 개시의 실험 가능성을 연구하는 것이다.

방법 및 결과

스웨덴의 두 지역에서 75-76세 인구의 절반이 심방세동의 선별검사에 초청되었다. 이전에 심방세동 진단을 받은 적이 없는 참가자들은 2주에 걸쳐 간헐적 심전도 검사를 받았다. 심방세동이 발견된 경우 참가자에게 항응고제를 제공하였다. 28개월 동안 13,331명의 주민이 초청되었으며, 이들 중 7,173명 (53.8%)이 참가하였다. 참가자 중 218명 (3.0%; 95% CI, 2.7–3.5)이 과거 심방세동에 대해 모르고 있었으며, 이들 중 37명 (전체 선별 인구 중 0.5%)은 그들의 첫 심전도에서 심방세동이 관찰되었 다. 간헐적인 심전도 검사는 신규 심방세동 진단을 4배 증가시켰다. 심방세동의 과거력은 9.3% (666명; 95% CI, 8.6–10.0)에서 알고 있었다. 선별검사를 받은 인구 중 심방세동 유병률은 12.3%였다. 이미 심방세동을 알고 있는 참가자 중 149명 (2.1%; 95% CI, 1.8–2.4)은 항응고제 치료를 받고 있지 않았다. 선별검사를 받은 전체 인구 중에서는 5.1% (95% CI, 4.6–5.7)가 심방세동에 대해 치료를 받고 있지 않았다. 선별검사로 3.7% (95% CI, 3.3–4.2)에서 항응고제 치료를 시작하였다. 과거에 심방세동을 진단받지 않았던 참가자 중 90% 이상에서 항응고제 치료 개시를 수용하였다.

결론

75-76세 연령층에 대한 대규모 선별검사에서 상당히 많은 참가자가 심방세동 치료를 받고 있지 않음을 알 수 있었다. 새로운 진단 받은 심방세동 환자에서 뇌출혈 예방 치료의 개시는 매우 성공적이었다.