Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study

Running title: Svennberg et al.; Mass Screening for Untreated Atrial Fibrillation

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Abstract

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

Methods and Results—Half of the 75/76-year-old population in two Swedish regions were invited to a screening program for AF. Participants without a prior diagnosis of AF underwent intermittent ECG recordings over two 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, n=218, 3.0% (95% confidence interval (CI) 2.7-3.5%) were found to have previously unknown AF, of these 37 (0.5% of the screened population) were found on their first ECG. The use of intermittent ECGs increased new AF detection 4-fold. A prior diagnosis of AF was known in 9.3%, (CI 8.6-10.0%, n=666). Total AF prevalence in the screened population was 12.3%. Of participants with known AF n=149 (2.1%, CI 1.8-2.4%) had no OAC treatment. In total, 5.1% (CI 4.6-5.7%) of the screened population had untreated AF; screening resulted in initiation of OAC treatment in 3.7% (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 75/76-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 Information—ClinicalTrials.gov. Identifier: NCT01593553.

Key words: atrial fibrillation, screening, prevention, stroke, anticoagulation
Background

The prevalence of atrial fibrillation (AF) has been estimated to be over 3% in the adult population\(^1\). Atrial fibrillation can be asymptomatic and intermittent, making diagnosis difficult. Camm et al.\(^2\) have suggested that asymptomatic AF represents a third of the total AF population, a result confirmed in pacemaker studies\(^3\).

The most feared complication in AF patients is ischemic stroke, a risk independent of the nature of AF\(^3-6\). Instead risk factor assessment (CHA\(_2\)DS\(_2\)-VASc score) is used to identify individuals with AF at risk of ischemic stroke\(^7\). The CHA\(_2\)DS\(_2\)-VASc score takes into account congestive heart failure, hypertension, age, diabetes, previous stroke/transient ischemic attack (TIA), vascular disease and female gender. At age 75 and above, current guidelines from the European Society of Cardiology (ESC) recommend oral anticoagulation (OAC) treatment for AF regardless of other risk factors\(^7\). OAC treatment reduces the risk of ischemic stroke by 64–70%\(^7,8\) but under-treatment remains a significant clinical problem\(^9,10\).

In the latest ESC guidelines, opportunistic screening for AF is recommended\(^7\).

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

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

Methods

Study population

The study design was described in a prior publication\(^11\). Individuals born in 1936/1937 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 randomisation was performed in the 75/76-year old population using stratification for gender, year of birth, and region. If randomized to the screening arm an invitation to participate in an AF screening program was sent by mail. Non-responders received one reminder in Halland and two reminders in Stockholm. Individuals who died before or during the invitation process were identified and excluded, see Figure 1. Information regarding nationality at birth was obtained from the Swedish Central Bureau of statistics.

**Screening procedure**

Participants were informed orally and in writing at a screening centre, and signed informed consent forms before entering the study. Prior medical history including AF, stroke/TIA, heart failure, hypertension, diabetes, myocardial infarction or vascular disease was obtained, and whether they were on OAC or anti-platelet 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 two weeks. An “index ECG” for detection of permanent arrhythmia was obtained. A one-lead ECG recorder from Zenicor (www.zenicor.com) with an integrated mobile transmitter that sends 30 s ECG strip data to a database was used. Participants placed their thumbs on the device twice daily, and in case of palpitations. The device has shown higher sensitivity for detection of AF than conventional 24 h Holter recordings12-14. In cases of inconclusive ECG tracings, participants were offered additional ECG recordings according to the investigating cardiologist’s judgement.
Definition of AF

Atrial fibrillation was defined as at least one 30-second recording with irregular rhythm without p-waves, or a minimum of two similar episodes lasting 10–29 seconds during two 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 where 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.

Statistical Methods

Continuous variables are reported as means ± SD. For continuous variables, Student’s t-test was used. For proportions, Fisher’s exact test or chi-square tests were used. Ordinal data was analysed using Mann-Whitney U or Kruskal-Wallis. Two-tailed tests were applied. A multivariable analysis was performed using logistic regression. The discriminative ability of the model was estimated as c statistics. A probability value of < 0.05 was regarded as significant.

These analyses were performed using IBM SPSS statistics version 22 software (IBM SPSS Statistics, IBM Corporation, Somers, New York), and Open-Epi (Open Source Epidemiologic 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. ClinicalTrials.gov identifier: NCT01593553.

Results

Participation

Screening started in March 2012 and concluded in June 2014. In total, 14 387 inhabitants were invited to take part in screening. Before the invitation process was completed 1056 individuals deceased. The remaining individuals’ response was 54% (7173 participants), which increased with additional invitations (see online supplement, supplemental figure 1).

The participants registered 189 715 ECG recordings, with an average of 26.4/subject. Only 1% made fewer than 15 ECG recordings. Because of difficulties in diagnosing AF from the recordings 3.5% of participants were referred for 24-h monitoring. Two patients withdrew their consent to participate. Referral for further workup was made in 10 patients due to high-grade AV 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%, CI 2.7-3.5%). A previous diagnosis of AF was present in 666 patients (9.3%, CI 8.6-10.0%), the majority of whom were men (n=407, 61.6%). Among those with known AF 517/666 (77.6%) were using OACs at the index visit. Thus, 149 patients with known AF were not using OACs, constituting 2.1% (CI 1.8-2.4%) of the screened population. Hence the prevalence of untreated AF was 5.1% (CI 4.6-5.7%).

In participants who got a new diagnosis of AF the mean number of registrations with AF was 4.5 (CI 3.4-5.6). In 40 individuals the diagnosis was made from one single pathological
registration during intermittent screening (Figure 2). In 12 individuals AF was diagnosed from two or more episodes ranging 10-29 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 four times as many with new AF compared to the index ECG (see online supplement, supplemental figure 2).

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 was previously known.

Use of oral anticoagulants

Men with known AF were more often treated with OACs (80.8% vs. 72.4%, p<0.05). In summary, 5.1% (CI 4.6-5.7%) of the participants in screening had AF and were 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 70/149 (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% (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 oral anticoagulants 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 get a new diagnosis of AF (Table 1, and online supplemental figure 3).

Participants with new AF were in general significantly taller, and heavier, with a higher body mass index (BMI) compared to 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 prior stroke/TIA, diabetes mellitus, height (OR per cm increase) and weight (OR per kg increase), see table 2.

Prior studies16,17 have used risk scores to predict the development of AF. We calculated a modified score based on the work of CHARGE-AF16 consortium, using height, weight, history of diabetes, 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 if there was any group that would not benefit from screening a multivariable analysis was performed to compare risk factors for participants where AF was detected compared to the no detection of AF group (see online supplement table 1). Female gender, lower weight, and absence of vascular disease came out as significantly associated with no detection of AF. In women with BMI<25 screening yielded only 1.3 % new AF.
Regional differences

Participation in the screening program was higher in rural Halland than in urban Stockholm (64% vs. 52%, p<0.001), and AF was a more commonly found in Halland (4.0% vs. 2.8% p=0.02). In Halland, individuals with known AF were more likely to be on OACs (87% vs 75%, p=0.001). See online supplemental table 2.

Discussion

This is the first multicentre prospective population-based systematic AF screening study using intermittent ambulatory ECG recordings in order to screen not only for 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 furthermore the first study with plans for long-term follow-up and a thorough study on health economy. New AF was found in 3.0% (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% (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. Protective OAC treatment because of untreated AF was initiated in 3.7% of the screened population.

Inclusion & uptake

Compared with established screening programs in Sweden participation was lower\textsuperscript{18-20}. However, participation in epidemiological studies has shown a declining trend\textsuperscript{21}, and compared to participation in another large research study in Sweden our participation was higher\textsuperscript{22}. Factors that could explain a lower participation are 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\textsuperscript{23}. The invitation was written in Swedish, which could exclude non-Swedish speaking participants.

**Prevalence & Prediction of AF**

Prior screening studies for AF have focused on strategies using screening for AF at one single time point, which is likely to detect only permanent arrhythmia, and is likely to miss most patients with paroxysmal arrhythmia. Intermittent ECG recording has shown a higher detection rate of AF compared to 24-h Holter monitoring\textsuperscript{13}. In a meta-analyses screening programmes using one single ECG recording found new AF in 1.4% of subjects >65 years\textsuperscript{24}. The current recommendation in the ESC guidelines for opportunistic screening for AF is based on a study comparing opportunistic ECG screening using pulse-palpation, where they found 1.64% new AF, with systematic screening using 12-lead ECGs where 1.62% new AF was found in a population with mean age 75\textsuperscript{7,23}. Our study found 0.5% new AF via the initial ECG recording (online supplementary figure 2) but with intermittent systematic screening detection of new AF increased 4-fold to 3% of the screened population, which is almost double the prevalence of prior studies where single time point ECG screening was performed\textsuperscript{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 on in their AF career, before AF becomes permanent\textsuperscript{15}.

Prior to intermittent ECG screening the screened population reported a prevalence of AF that was 9.3%. This is a higher prevalence of AF compared to studies of populations of similar age groups in North-America\textsuperscript{25,26}, in the UK\textsuperscript{27} and Greece\textsuperscript{28} and slightly lower than Icelandic
and Dutch prevalence studies. Systematic screening for AF in populations of a similar ethnicity where the prevalence of known AF is lower would likely yield a higher rate of newly discovered AF, which would further increase 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, but as the population ages and the prevalence of risk factors for AF increases, AF prevalence is likely to rise in these areas, 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, prior stroke/TIA and diabetes mellitus. Our results are consistent with results from the Framingham study where congestive heart failure was also shown to be one of the most important risk factors for atrial fibrillation with a 4.5- and 5.9-fold increase of risk in men, and women respectively, whereas diabetes conferred a respective risk of 1.4 and 1.6. A prior history of stroke/TIA was also a predictor for AF. These patients should already have been screened for AF using 24-h Holter monitoring according to current European stroke guidelines unless another cause for stroke was apparent. This short monitoring period, which differs from the more extended screening for AF in the AHA guidelines, presumably leads to under-detection of AF.

Individuals with vascular disease were diagnosed with new AF to a greater extent, despite that they most likely had already been subjected to cardiovascular work-up (increasing the probability that AF should have been diagnosed). This could signify that individuals with vascular disease are more prone to get AF, but also shows what a difficult endpoint AF is due to its asymptomatic and intermittent nature. Participants who weighed more, were taller, and had
a higher BMI were more likely to get a diagnosis with AF, which is in accordance with prior studies\textsuperscript{16,38}.

In women with BMI\textless{}25 only 1.3\% new AF was found. This might indicate that in women AF screening might be initiated at a higher age as the prevalence of AF is lower in women compared to men in the same age category\textsuperscript{9}. However, women have a higher risk of stroke compared to men\textsuperscript{39}, so continuing screening at the same age as men might still be of pertinent as the individuals found are at a higher risk.

Participants with known AF had more co-morbidity. Increasing CHA\textsubscript{2}DS\textsubscript{2}-VASc scores correlate with an increased presence of AF (Fig. 5).

In a pilot study, individuals aged 75 with at least one additional risk factor for stroke underwent screening for silent AF using intermittent ECG registration\textsuperscript{40}. Previously untreated AF was found in 7\% of the participants. In the pilot study, patients with newly diagnosed AF had a CHA\textsubscript{2}DS\textsubscript{2}-VASc mean score of 3.85, median 4, and in the present study the respective scores were 3.47/3. This difference (p=0.03) in co-morbidity may explain some of the difference in AF prevalence\textsuperscript{40}.

\textbf{Initiation of OAC treatment}

In patients with new AF, acceptance of treatment with OACs despite lack of symptoms was high. A possible reason is that cardiologist with special interest in AF did the workup. Over 70\% of participants chose treatment with novel oral anticoagulants (NOACs).

Compared with prior studies\textsuperscript{9,41,42} participants with known AF were on OAC treatment to a greater proportion than expected. The invitation stated that patients with AF would be referred for OAC treatment; hence patients with a negative attitude towards 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 to 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 realising 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 do. In this study almost 20% of individuals with known AF were treated with aspirin, despite poor effect on stroke-prevention in individuals with AF\(^8,43\). In an AF population less well treated with OAC, it is probable that systematic screening could yield further increase in OAC treatment among participants.

**Regional differences**

In Halland screening uptake was greater, which could partly be explained by decentralized organisation of screening compared with Stockholm’s centralized organization. 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 vs 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 atrial
fibrillation using intermittent ECG recordings. They predict that the STROKESTOP screening program will imply a cost of €4,164 per QALY when using a lifelong perspective, which is regarded as a low cost per QALY. It could hence be implied, that in a 75/76-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 (see online supplemental table 3) which should be fulfilled in order to justify mass screening. AF meets all of these criteria. When screening for malignancies conditions that might not impact on the patients’ life expectancy or symptoms might be found. In contrast, when 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 in screening for atrial fibrillation.

**Limitations**

By limiting the registration period to 14 days and monitoring the participants only <1‰ of the time, there was probably under-detection of AF. A patient who has AF detected by 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 less acceptable to the participants.

Atrial flutter can remain undiagnosed, as its detection can be difficult using this method. As atrial flutter is an arrhythmia more commonly observed in blacks compared to 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
Most clinicians unfailingly agree to initiate OAC treatment in individuals with asymptomatic AF and increased CHA\textsubscript{2}DS\textsubscript{2}-VASc score if AF is found en passant on a regular health check, and a recent study of stroke risk in incidentally discovered AF supports this\textsuperscript{50}. 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 one episode of AF, and 12 individuals presented with 2 or more episodes of AF shorter than 30 seconds, likely representing a low AF burden. In studies using continuous monitoring, such as the ASSERT study, no clear temporal relationship between duration of AF and stroke has been seen\textsuperscript{3,51}. In a recent study of patients with cardiac implanted devices a threshold of \( \geq 5 \) min during a median monitoring period of 24 months was statistically significantly associated with the occurrence of ischemic stroke\textsuperscript{52}. However, AF of shorter duration than 5 minutes was not studied. Compared to continuous monitoring the finding of AF on intermittent monitoring is likely to signify a high AF burden, as the monitoring represents a short temporal time frame.

Self-reporting of risk factors could lead to partly erroneous reporting of co-morbidity, but in our pilot study, patient information on (self-reported) co-morbidity was accurate in 99% of cases\textsuperscript{40}.

Studies comparing AF prevalence across different racial groups have shown heterogeneity with higher prevalence in whites compared to black, Hispanic and Asian populations\textsuperscript{53,32,49,54}. This difference remains even if AF prevalence is studied in pacemaker studies, where differences in health care consumption patterns are of no importance\textsuperscript{54}. Even though AF was less-common in blacks compared to whites in a study of an American bi-racial population, stroke remained a vast problem, with higher incidence rates than in the white
population\textsuperscript{55}, raising the possibility that the importance of AF as a risk factor for stroke might vary between ethnical groups.

Our data describes a population where 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 question if 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-time, using data from the national health registries, and the national prescription registries, to observe if intermittent screening for AF and initiating of OAC treatment will reduce the risk of stroke as compared to the non-screened population.

Conclusions

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

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**References:**


**Table 1. Baseline characteristics at study entry.**

<table>
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<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>
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<tr>
<td>Congestive heart failure</td>
<td>124 (19.5%)</td>
<td>6 (2.8%)</td>
<td>117 (1.9%)</td>
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<td>Hypertension</td>
<td>389 (59.4%)</td>
<td>113 (52.1%)</td>
<td>3064 (48.9%)</td>
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<td>Diabetes mellitus</td>
<td>135 (20.3%)</td>
<td>29 (13.3%)</td>
<td>630 (10.0%)</td>
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<td>Prior Stroke/TIA</td>
<td>137 (20.7%)</td>
<td>21 (9.6%)</td>
<td>490 (7.9%)</td>
<td>0.309</td>
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<td>Vascular disease</td>
<td>115 (17.5%)</td>
<td>31 (14.3%)</td>
<td>518 (8.3%)</td>
<td>0.004</td>
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<tr>
<td>Female Gender</td>
<td>254 (38.4%)</td>
<td>99 (45.4%)</td>
<td>3496 (55.7%)</td>
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<td><strong>CHA2DS2-VASc</strong></td>
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<td></td>
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<td>0.392</td>
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<tr>
<td>Mean +/- sd</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CHA2DS2-VASc Median (IQR)</td>
<td>4 (2)</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>0.42</td>
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<td>OAC treatment</td>
<td>517 (77.6%)</td>
<td>5 (2.3%)</td>
<td>99 (1.6%)</td>
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<td>Aspirin</td>
<td>122 (18.3%)</td>
<td>54 (24.8%)</td>
<td>1452 (23.1%)</td>
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<td>Height, cm (SD)</td>
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<td></td>
<td></td>
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<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>
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<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>
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<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>
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<tr>
<td>Weight, kg (SD)</td>
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<tr>
<td>All</td>
<td>81.6 (17.0)</td>
<td>81.4 (18.0)</td>
<td>74.7 (14.0)</td>
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<td>Women</td>
<td>72.3 (13.5)</td>
<td>79.7 (23.3)</td>
<td>68.9 (13.0)</td>
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<td>Men</td>
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<td>82.5 (13.6)</td>
<td>81.3 (12.1)</td>
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<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 (9.2)</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>

*Comparisons done between Newly diagnosed AF and No AF.
TIA= Transient Ischaemic Attack, BMI= Body Mass Index
Table 2. Multivariable analysis for development of AF.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimated β (SE)</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure (Yes)</td>
<td>1.973 (0.168)</td>
<td>7.19 (5.18 - 9.98)</td>
<td>0.000</td>
</tr>
<tr>
<td>Hypertension (Yes)</td>
<td>0.136 (0.091)</td>
<td>1.15 (0.96 - 1.37)</td>
<td>0.140</td>
</tr>
<tr>
<td>Diabetes Mellitus (Yes)</td>
<td>0.375 (0.126)</td>
<td>1.46 (1.14 - 1.86)</td>
<td>0.000</td>
</tr>
<tr>
<td>Prior stroke/TIA (Yes)</td>
<td>0.821 (0.125)</td>
<td>2.27 (1.78 - 2.9)</td>
<td>0.000</td>
</tr>
<tr>
<td>Vascular disease (Yes)</td>
<td>0.199 (0.137)</td>
<td>1.22 (0.93 - 1.6)</td>
<td>0.150</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>-0.037 (0.132)</td>
<td>0.96 (0.74 - 1.25)</td>
<td>0.780</td>
</tr>
<tr>
<td>Height, cm</td>
<td>0.031 (0.008)</td>
<td>1.03 (1.02 - 1.05)</td>
<td>0.000</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>0.014 (0.003)</td>
<td>1.01 (1.01 - 1.02)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Odds ratio calculated for height calculated per 1 cm increase and weight per 1 kg increase
AF= Atrial Fibrillation, TIA= transient ischaemic attack

Figure Legends:

Figure 1. Participation in systematic screening for atrial fibrillation in a 75/76-year old population.

Figure 2. Number of AF episodes recorded by intermittent ECG in individuals diagnosed with new AF.

Figure 3. Time to first detection of AF among participants undergoing intermittent ECG registrations.

Figure 4. Initiation of OAC treatment.

Figure 5. Association between CHA2DS2-VASc score and prevalence of AF, p<0.001 (Kruskal-Wallis).
Stockholm + Halland County  
\( n = 28\,768 \)

1:1 Randomization

Prospectively randomized to screening  
\( n = 14\,387 \)

Not screened  
\( n = 14\,381 \)

Died before completed invitation  
\( n = 1056 \)

Individuals invited to screening  
\( n = 13\,331 \)

Not participating  
\( n = 6158 \)

Participation in screening  
\( n = 7173 \)

Figure 1
Figure 2
Figure 3
Participants in screening
n=7173

New AF
n=218

Untreated
n=213

OAC not initiated:
Patient preference, n=6
Contra-indications; Malignancy, n=2
GI-bleed, n=1
Dementia, n=2
Severe co-morbidity, n=3
Other, n=1

OAC initiated
n=198

Known AF
n=666

Untreated
n=149

On OAC
n=517

OAC not initiated:
Patient preference, n=36
Doctor’s preference, n=6
Contra-indications; Malignancy, n=2
GI bleed, n=6
ICH, n=3
Severe co-morbidity, n=10
Lost to F/U, n=15
Still undecided, n=1

Figure 4
Figure 5
Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study
Emma Svennberg, Johan Engdahl, Faris Al-Khalili, Leif Friberg, Viveka Frykman and Mårten Rosenqvist

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### Supplemental Material

**Supplemental Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimated ß (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.
<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 be 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

![Bar chart showing clinical characteristics comparison between newly diagnosed AF and no AF participants.](image-url)
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. 28개월의 동기 기간 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 관절력은 9.3%(666명; 95% CI, 8.6–10.0)에서 알게 되었다. 선별검사를 받은 인구 중 심방세동 유병률은 12.3%였다. 이에 심방세동을 알게 된 참가자 중 149명(2.1%; 95% CI, 1.8–2.4)은 항응고제 치료를 받지 않았다. 선별검사를 받은 전체 인구 중에서는 5.1%(95% CI, 4.6–5.7)가 심방세

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