

SCIENTIFIC STUDIES

ZENICOR

The Zenicor  
Solution  
**Scientific  
studies**

**Zenicor**  
MEDICAL SYSTEMS



## Our mission

No one should suffer a stroke  
due to an undiagnosed  
atrial fibrillation.

### **Zenikor Medical Systems AB**

Saltmätargatan 8  
113 59 Stockholm  
+46-8-442 68 60  
[www.zenikor.se](http://www.zenikor.se)  
[info@zenikor.com](mailto:info@zenikor.com)

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# Research with the Zenicor Solution

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***Zenicor Medical Systems AB was founded in 2003 and has since then been established as one of the lead players in the fields of early diagnosis of arrhythmias and stroke prevention.***

A large number of research studies spanning from pediatric cardiology to early diagnosis of arrhythmias, cost-effectiveness and Data-driven screening have been performed since the start. These studies have established good diagnostic ability, in many cases clearly superior to conventional methods, and excellent results in terms of health economics. In addition to this, the research results have led to new, more efficient work methods for the healthcare.

An effective method to prevent stroke using the Zenicor Solution for primary preventive atrial fibrillation screening has been developed and tested. The screening research has attracted a great deal of attention globally and has led the way for atrial fibrillation screening. New ways to make screening more effective and cost-effective are still being explored together with top-researchers in the field.

Additionally a new and effective carepathway for patients presenting with symptoms of arrhythmias in primary care has been developed. A new workflow that digitalises the care pathway and makes care more accessible for the patient, which facilitates a quicker diagnosis. Research with the Zenicor Solution has been conducted at universities and hospitals in Sweden, Denmark, Norway, Switzerland, Austria, Germany and the UK. This brochure is a compilation of published research where the Zenicor Solution has been used and evaluated. A complete list of published research is found at the end of the brochure.

# Arrhythmia assessments **In adults**

# Intermittent short ECG recording is more effective than 24-hour Holter ECG in detection of arrhythmias (Prima Rytm study)

*Hendrikx T, Rosenqvist M, Wester P, Sandström H & Hörnsten R. BMC Cardiovascular Disorders, 2014.*

## Background

Many patients report symptoms of palpitations or dizziness/presyncope. These patients are often referred for 24-hour Holter ECG, although the sensitivity for detecting relevant arrhythmias is comparatively low. Intermittent short ECG recording over a longer time period might be a convenient and more sensitive alternative. The objective of this study is to compare the efficacy of 24-hour Holter ECG with intermittent short ECG recording over four weeks to detect relevant arrhythmias in patients with palpitations or dizziness/presyncope.

## Methods

Design: prospective, observational, cross-sectional study. Setting: Clinical Physiology, University Hospital. Patients: 108 consecutive patients referred for ambiguous palpitations or dizziness/presyncope. Interventions: All individuals underwent a 24-hour Holter ECG and additionally registered 30-second handheld ECG (Zenicor EKG® thumb) recordings at home, twice daily and when having cardiac symptoms, during 28 days. Main outcome measures: Significant arrhythmias: atrial fibrillation (AF), paroxysmal supraventricular tachycardia (PSVT), atrioventricular (AV) block II–III, sinus arrest (SA), wide complex tachycardia (WCT).

## Results

95 patients, 42 men and 53 women with a mean age of 54.1 years, completed registrations. Analysis of Holter registrations showed atrial fibrillation (AF) in two patients and atrioventricular (AV) block II in one

patient (= 3.2% relevant arrhythmias [95% CI 1.1–8.9]). Intermittent handheld ECG detected nine patients with AF, three with paroxysmal supraventricular tachycardia (PSVT) and one with AV-block-II (= 13.7% relevant arrhythmias [95% CI 8.2–22.0]). There was a significant difference between the two methods in favour of intermittent ECG with regard to the ability to detect relevant arrhythmias ( $P=0.0094$ ). With Holter ECG, no symptoms were registered during any of the detected arrhythmias. With intermittent ECG, symptoms were registered during half of the arrhythmia episodes.

### Conclusions

Intermittent short ECG recording during four weeks is more effective in detecting AF and PSVT in patients with ambiguous symptoms arousing suspicions of arrhythmia than 24-hour Holter ECG.

## Identification of paroxysmal, transient arrhythmias: Intermittent registration more efficient than the 24-hour Holter monitoring

*Hendrikx T, Rosenqvist M, Sandström H, Persson M & Hörnsten R. Läkartidningen, 2015.*

### Abstract

Many patients suffer from palpitations or dizziness/presyncope. These patients are often referred for Holter ECG (24 hour), although the sensitivity for detecting arrhythmias is low. A new method, short intermittent regular and symptomatic ECG registrations at home, might be a convenient and more sensitive alternative also suitable for primary health care. In this case report we present a patient who had contacted health care several times during a seven year period for paroxysmal palpitations. Routine examination with 24 hour Holter ECG and event

recorder did not result in a diagnosis. Using intermittent handheld ECG registration at home, a paroxysmal supraventricular arrhythmia was diagnosed. Further investigation revealed that the patient had a concealed Wolff-Parkinson-White (WPW) syndrome.

## **Feasibility of patient managed ECG recordings to detect the time of atrial fibrillation recurrence after electrical cardioversion; Results from the PRE-ELECTRIC Study**

SCIENTIFIC STUDIES

*Andersen E L, Solberg M G, Walle-Hansen M M, Enger S, Onarheim S, Olufsen M, Berge T, Christophersen I E, Ulmoen S R & Tveit A, 2023.*

### **Background**

Electrical cardioversion (ECV) is a common procedure to terminate persistent atrial fibrillation (AF). The recurrence rate is high, and the patients often fail to recognize AF recurrence.

### **Objectives**

The aim of the study was to evaluate the feasibility of patient-managed electrocardiography (ECG) to detect the time to AF recurrence after ECV.

### **Methods**

PRE-ELECTRIC (predictors for recurrence of atrial fibrillation after electrical cardioversion) is a prospective, observational study. Patients  $\geq 18$  years of age scheduled for ECV of persistent AF at Bærum Hospital were eligible for inclusion in the study. Time to recurrence of AF was detected by thumb ECG, recorded twice daily and whenever experiencing symptoms. The observation period was 28 days. We defined ad-



herence as the observed number of days with ECG recordings divided by the expected number of days with ECG recordings. Study personnel contacted the participants by phone to assess their awareness of AF recurrence after a recurrence was detected in the thumb ECG.

## Results

The study enrolled 200 patients scheduled for ECV of persistent AF at Bærum Hospital between 2018 and 2022. The mean age was  $66.2 \pm 9.3$  years, and 21.0% (42/200) were women. The most frequent comorbidities were hypertension ( $n = 94$ , 47.0%) and heart failure ( $n = 51$ , 25.5%). A total of 164 participants underwent ECV of AF. The procedure was initially successful in 90.9%, of which 50.3% had a recurrence of AF within 4 weeks. The median time to recurrence was 5 days. Among the cardioverted participants, 123 (75.0%) had no missing days of thumb ECG recording during the observation period, and 97.0% had  $\leq 3$  missing days. More than a third (37.3%) of the participants with AF recurrence were unaware of the recurrence at the time of contact. Women were older and more symptomatic than men but had similar outcomes after ECV. Conclusions: Recurrence of AF after ECV was common. Using patient-managed thumb ECG was a feasible method to detect AF recurrence following ECV. Further studies are needed to investigate whether patient-managed ECG after ECV can optimize AF treatment.





# Arrhythmia assessments **In children**

# Handheld ECG in analysis of arrhythmia and HRV in children with Fontan circulation

*Alenius Dahlqvist J, Karlsson M, Wiklund U, Hörnsten R & Rydberg A. Journal of electrocardiology, 2014.*

## **Background**

Our aim was to evaluate the intermittent use of a handheld ECG system for detecting silent arrhythmias and cardiac autonomic dysfunction in children with univentricular hearts.

## **Methods**

Twenty-seven patients performed intermittent ECG recordings with handheld devices during a 14-day period. A manual arrhythmia analysis was performed. We analyzed heart rate variability (HRV) using scatter plots of all interbeat intervals (Poincaré plots) from the total observation period. Reference values of HRV indices were determined from Holter-ECGs in 41 healthy children.

## **Results**

One asymptomatic patient had frequent ventricular extra systoles. Another patient had episodes with supraventricular tachycardia (with concomitant palpitations). Seven patients showed reduced HRV.

## **Conclusions**

Asymptomatic arrhythmia was detected in one patient. The proposed method for pooling of intermittent recordings from handheld or similar devices may be used for detection of arrhythmias as well as for cardiac autonomic dysfunction.

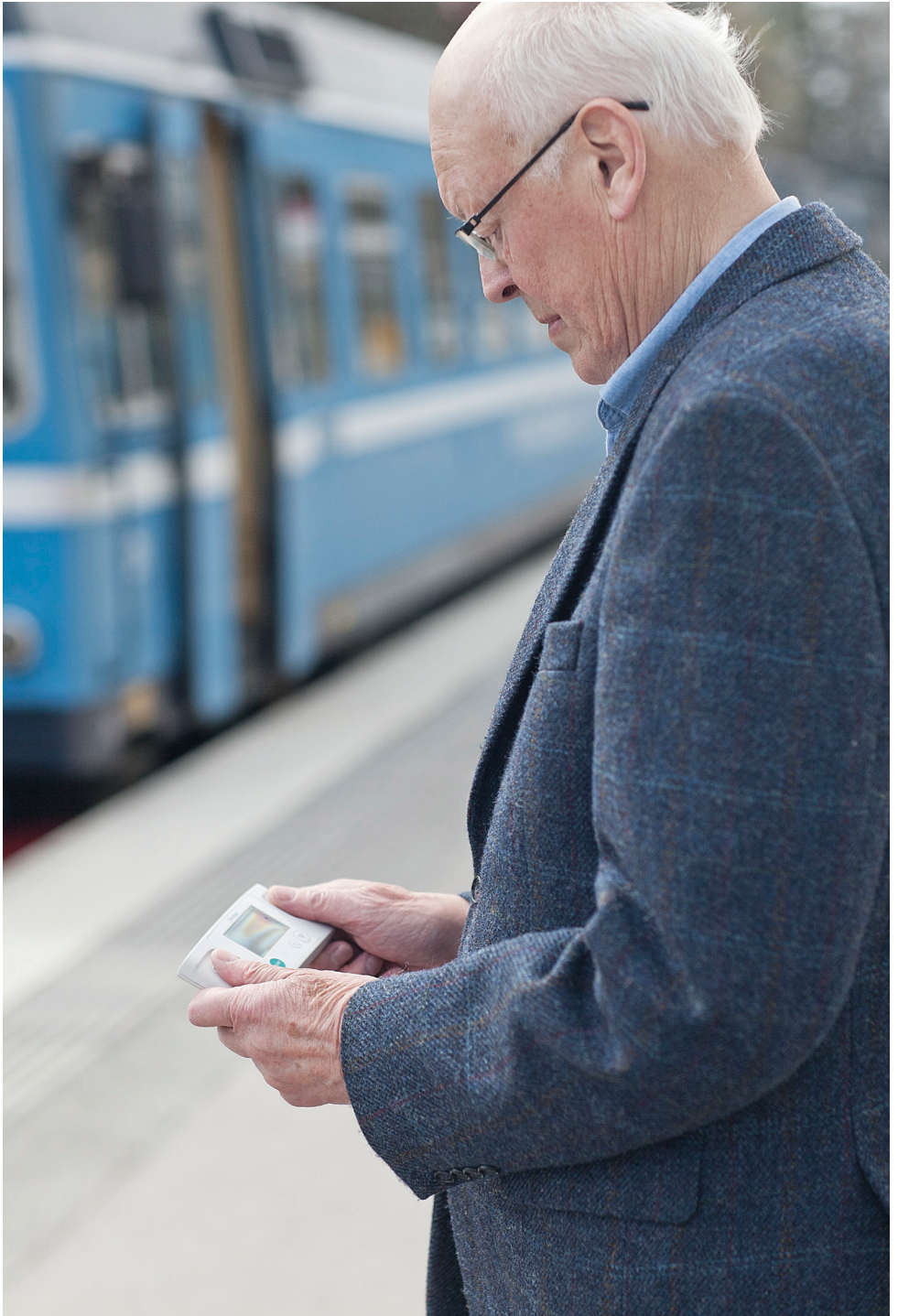
# Arrhythmia Detection in Pediatric Patients: ECG Quality and Diagnostic Yield of a Patient-Triggered Einthoven Lead-I Event Recorder (Zenicor EKG-2™)

*Usadel L, Haverkämper G, Herrmann S, Löber R, Weiss K, Opgen-Rein B, Berger F, Will JC. Arrhythmias Detection in Pediatric Patients: ECG Quality and Diagnostic Yield of a Patient-Triggered Einthoven Lead-1 Event Recorder (Zenicor EKG-2) Pediatric Cardiology, 2015.*

## **Abstract**

Symptoms that may be caused by arrhythmia are common in pediatric outpatient departments, though it remains challenging to reveal paroxysmal tachycardia. This investigation evaluated prospectively the quality and diagnostic yield of a newly available handheld patient-activated event recorder (ER) in children. In 226 children (pts) aged 0–17 years with or without congenital heart defects, pacemaker/ICDs or arrhythmia, a lead-I ER ECG was created. ER ECGs were recorded by pressing the patients' thumbs on the device and were analyzed in comparison with a lead-12 ECG, as gold standard.

Event recording and data transmission were possible in all cases. ECG quality of the ER showed a high accordance in measuring heart rate (ICC = 0.962), duration of QRS complexes ( $\kappa$  = 0.686), and PR interval (ICC = 0.750) ( $p < 0.001$ ) although P wave detection remained challenging ( $p = 0.120$ ). 36 % ( $n = 82$ ) of the pts had heart rhythm disturbances. The ER yielded 92 % sensitivity in diagnosing supraventricular tachycardia plus 77 % sensitivity and 92 % specificity in identifying abnormal ECGs. In children, the application of the tested ER was suitable. ECGs of good quality could be performed and transmitted easily, and also complex arrhythmia analysis was possible. This ER is an excellent diagnostic device for the detection and exclusion of tachycardia in children.



# Secondary **stroke** prevention

# Screening of Paroxysmal Atrial Fibrillation after Ischemic Stroke: 48-Hour Holter Monitoring versus Prolonged Intermittent ECG Recording

Orrsjö G, Cederin B, Bertholds E, Nasic S & Welin L. *ISRN Stroke, Volume, 2014.*

## Aims

Screening of paroxysmal atrial fibrillation (PAF) after ischemic stroke and TIA is important. The ideal method is not known and studies of intermittent screening methods in particular are lacking. In this retrospective study we compared a shorter continuous screening method with an intermittent screening method.

## Methods

Since early 2011 our stroke unit has used two different methods of screening: either a 48-hour continuous screening with Holter monitor or a 21-day twice daily intermittent screening with a hand-held ECG recorder. Through the Swedish National Stroke Registry and medical records reviewing all screening episodes between 2011-02-01 and 2013-01-31 were collected and analysed.

## Results

Of 386 screenings, 26 screenings were excluded leaving 360 screenings for the final analysis of which 114 screenings were made with hand-held ECG recorder and 246 with Holter monitoring. No significant difference between the groups concerning basic characteristics was observed. In the hand-held ECG recorder group a total of 13 PAF screenings (11.4%) were detected compared with 7 (2.8%) in the Holter group ( $P=0,001$ ).



## Conclusions

A prolonged intermittent screening is a better method than a shorter continuous screening in terms of detecting PAF after ischemic stroke and TIA.

# Improved screening for silent atrial fibrillation after ischaemic stroke (Propp-Stopp)

*Sobocinski Doliwa P, Rooth Änggårdh E, Frykman Kull V, von Arbin M, Wallén H & Rosenqvist M. Europace, 2012.*

## Objectives

To what extent silent paroxysmal atrial fibrillation (AF) is present in ischaemic stroke patients has not been established. We hypothesized that brief intermittent long-term electrocardiogram (ECG) recordings at regular time intervals are more effective than short-term continuous ECG monitoring in detecting silent AF episodes.

## Methods and Results

Consecutive patients who had suffered an ischaemic stroke/ transient ischaemic attack (TIA) and were without known AF underwent a 24 h continuous ECG recording and performed 10 s rhythm registrations using a hand-held ECG recorder twice daily for 30 days and when arrhythmia symptoms occurred. Two hundred and forty-nine stroke patients were included. Mean National Institute of Health Stroke Scale (NIHSS) score was 0.9 (0–10). In total, 17 patients were diagnosed with AF. One hundred and eight AF episodes were diagnosed in 15 patients using intermittent recording, out of which 22% were unscheduled symptom triggered episodes. In three patients AF was diagnosed with both methods and in two patients AF was detected exclusively with 24 h Holter monitoring. A significant difference in favour of the hand-held ECG was shown between the two methods ( $P = 0.013$ ). The total prevalence of AF was 6.8% and increased to 11.8% in patients  $\geq 75$  years. No AF was found in patients  $< 65$  years.

## Conclusion

Prolonged brief intermittent arrhythmia screening substantially improves the detection of silent paroxysmal AF in patients with a recent ischaemic stroke/TIA, and thus facilitates the detection of patients who should receive oral anticoagulant treatment.

# Detection of Atrial Fibrillation with Intermittent Handheld Electrocardiogram in Patients with Ischemic Stroke and Transient Ischemic Attack

*Olsson A-S & Engdahl J. Journal of Stroke and Cerebrovascular Diseases, 2016.*

## Background

Atrial fibrillation is an important risk factor for recurrent ischemic stroke and transient ischemic attack. Despite routine investigation, some patients' atrial fibrillation remains undetected. Intermittent handheld electrocardiogram (ECG) is an option for extended ECG monitoring aiming at enhancing detection rates. This study aimed to explore the detection rate of atrial fibrillation in stroke and transient ischemic attack patients with intermittent handheld ECG in the clinical setting of Halland Hospital Halmstad.

## Methods

Patients discharged with a diagnosis of ischemic stroke or transient ischemic attack who underwent intermittent handheld ECG recording at Halland Hospital Halmstad from January 1, 2010, to March 31, 2014, were retrospectively studied; 370 patients in total. A positive investigation was defined as either atrial fibrillation for a minimum of 10 seconds or a short irregular supraventricular run.

## Results

We found an overall atrial fibrillation detection rate of 7.6% (95% CI 5.1%-10.1%). The detection rate in stroke patients (11.0%) was significantly higher than in transient ischemic attack patients (5.0%),  $P = .032$ . The detection rate in patients aged less than 65 years was 4.2%, increasing to 9.8% in patients aged 65 years or older,  $P = .051$ .

## Conclusion

This retrospective study shows an atrial fibrillation detection rate of 7.6% in a stroke and transient ischemic attack population using prolonged intermittent monitoring with handheld ECG recording. The compliance to the monitoring was excellent.

# Performance of short ECG recordings twice daily to detect paroxysmal atrial fibrillation in stroke and transient ischemic attack patients

*Poulsen M B, Binici Z, Dominguez H, Soja A M, Kruuse C, Hornnes A H, Rasmussen R S & Overgaard K. International Journal of Stroke, 2016.*

## Aims

Prolonged cardiac monitoring after stroke is recommended though there is no consensus on optimal methods. Short-term ECG recordings with a "thumb-ECG" device have shown promising preliminary results regarding effectiveness and cost benefit. We aimed to examine the performance of thumb-ECG and five days' Holter monitoring in a prospective trial. A secondary endpoint was the inter-observer agreement of the thumb-ECG.

## Methods and Results

Patients older than 65 years with no history of atrial fibrillation who suffered an acute stroke or transient ischemic attack of unknown origin were prospectively included. Patients were monitored for atrial fibrillation with five days' Holter and concurrent 30s thumb-ECG twice daily, the latter continuing for 30 days. Inter-observer agreement for the thumb-ECG was determined.

One hundred patients were included and 95 patients were analyzed. Paroxysmal atrial fibrillation was diagnosed in 20 patients with the thumb-ECG recordings and 17 patients on the Holter monitoring. Only 10 were diagnosed with both methods. The difference between the detection rates of the two devices was not significant ( $p=0.63$ ). The inter-observer agreement of the thumb-ECG had a kappa value of 0.65.

## Conclusion

Thirty days' thumb-ECG recordings twice daily for 30s detect a high proportion of paroxysmal atrial fibrillation in a stroke or transient ischemic attack cohort. The proportion was comparable to five days' Holter monitoring but the agreement between the two methods was poor and the trial was not powered to detect a minor difference between the devices. The inter-observer agreement for the thumb-ECG was substantial.

# Primary **stroke** prevention

# Screen-detected atrial fibrillation and 'micro-atrial fibrillation' and risk of cardiovascular events after myocardial infarction in elderly patients

*Berge T, Langeland Myhre P, Annesønn Kalstad A, Laake K, Tveit S H, Onarheim S, Solheim S, Seljeflot I, Arnesen H, Tveit A, Cardiology, 2022.*

## Background

Incident atrial fibrillation (AF) occurs in 5-10% of patients after acute myocardial infarction (AMI) and is associated with adverse outcomes. Guidelines now recommend screening for AF in all elderly patients. However, the relevance of screen-detected AF and short episodes of irregular supraventricular ectopic beats ('micro-AF') after AMI is unknown.

## Objectives

To investigate the value of two-week intermittent ECG screening to detect incident AF and 'micro-AF' in elderly patients 12 months after an AMI, and its association with risk of cardiovascular events.

## Methods

This was an investigator-initiated, multicenter substudy of the Omega-3 fatty acids in Elderly patients with Myocardial Infarction (OMEMI) trial, in Norway. Women and men aged 70-82 years, with a recent AMI, were recruited during 2012-2018. All participants had a 12-lead ECG performed at 3, 12 and 24 months. Patients without AF one year after the index AMI underwent 2 weeks of intermittent 30-second 'thumb ECG' screening. Incident AF and 'micro-AF' (episodes of  $\geq 3$  consecutive irregular supraventricular ectopic beats) were registered, and the association with risk of major cardiovascular events (MACE; non-fatal

AMI, stroke, coronary revascularization, hospitalization for heart failure, or all-cause death) was analyzed with logistic regression.

## Results

Among 1014 patients (198 (28.7%) women), 255 (25.1%) had known AF or AF identified at baseline. New-onset AF was detected clinically or at study visits in 39 (3.8%) patients. By screening participants without AF (n=567), unknown AF was identified in 4 (0.7%) and 'micro-AF' in 27 (4.8%) patients. Among 43 patients with incident AF, 21 (48.8%) experienced a MACE, which was significantly higher than those without AF (n=114, 15.9%;  $p<0.001$ ), driven by a higher risk of AMI or revascularization. Nine (33.3%) patients with 'micro-AF' and 75 (13.9%) without 'micro-AF' experienced a MACE ( $p=0.002$ ), explained mostly by a higher risk of heart failure hospitalization ( $p<0.001$ ). Using patients without AF and 'micro-AF' as reference, 'micro-AF' was associated with an intermediate risk of MACE (OR 2.8; 95% CI 1.2-6.4) and new-onset AF with a high risk of MACE (OR 5.3; 95% CI 2.8-10.0).

## Conclusions

Two-week intermittent ECG screening identified few cases of new-onset AF, but a substantial number of patients with 'micro-AF'. 'Micro-AF' was associated with an increased risk of major cardiovascular events, albeit with an intermediate risk compared to those with new-onset AF.

# Cluster randomised controlled trial of screening for atrial fibrillation in people aged 70 years and over to reduce stroke: protocol for the pilot study for the SAFER trial

*Williams K, Narendra Modi R, Dymond A, Hoare A, Powell A, Burt J, Edwards D, Lund J, Johnson R, Lobban T, Lown M, Sweeting M J, Thom H, Kaptoge S, Fusco F, Morris S, Lip G, Armstrong N, Cowie M R, Fitzmaurice D A, Freedman B, Griffin S J, Sutton S, Hobbs Fd R, McManus R J, Mant J, The Safer Authorship Group, 2022.*

## Introduction

Atrial fibrillation (AF) is a common arrhythmia associated with 30% of strokes, as well as other cardiovascular disease, dementia and death. AF meets many criteria for screening, but there is limited evidence that AF screening reduces stroke. Consequently, no countries recommend national screening programmes for AF. The Screening for Atrial Fibrillation with ECG to Reduce stroke (SAFER) trial aims to determine whether screening for AF is effective at reducing risk of stroke. The aim of the pilot study is to assess feasibility of the main trial and inform implementation of screening and trial procedures.

## Methods and analysis

SAFER is planned to be a pragmatic randomised controlled trial (RCT) of over 100 000 participants aged 70 years and over, not on long-term anticoagulation therapy at baseline, with an average follow-up of 5 years. Participants are asked to record four traces every day for 3 weeks on a hand-held single-lead ECG device. Cardiologists remotely confirm episodes of AF identified by the device algorithm, and general practitioners follow-up with anticoagulation as appropriate. The pilot study is a cluster RCT in 36 UK general practices, randomised 2:1 con-



trol to intervention, recruiting approximately 12 600 participants. Pilot study outcomes include AF detection rate, anticoagulation uptake and other parameters to incorporate into sample size calculations for the main trial. Questionnaires sent to a sample of participants will assess impact of screening on psychological health. Process evaluation and qualitative studies will underpin implementation of screening during the main trial. An economic evaluation using the pilot data will confirm whether it is plausible that screening might be cost-effective.

## **Feasibility of screening for atrial fibrillation in a domiciliary setting: opportunistic one-time screening at preventive home visits in municipalities**

*Poulsen P-B, Hemmingsen U, Melgaard T-A, Buch Elleby H, Wedell-Wedellsborg D, Dybro L, Lund I-M, Dixen U & Frost L. Scandinavian Cardiovascular Journal, 2022.*

### **Abstract**

Current evidence base for atrial fibrillation (AF) screening is insufficient. An important finding in the STROKESTOP study was that non-participants had significantly worse outcomes. In a group of potentially non-participants feasibility of opportunistic screening in a domiciliary setting with municipality preventive home visits to citizens >75 years was investigated. Handheld ECG device was used by trained municipality caregivers followed by cardiologist assessment. Eighty-five percent consented to being screened, and seven of 477 screened were found with AF. Opportunistic screening in preventive home visits had a high participation rate and was feasible. Randomized trials are needed before making any firm conclusions.

# **Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial**

*Svennberg E, Friberg L, Frykman V, Al-Khalili F, Engdahl J & Rosenqvist M. 2021.*

## **Aims**

Atrial fibrillation is a leading cause of ischaemic stroke. Early detection of atrial fibrillation can enable anticoagulant therapy to reduce ischaemic stroke and mortality. In this randomised study in an older population, we aimed to assess whether systematic screening for atrial fibrillation could reduce mortality and morbidity compared with no screening.

## **Methods**

STROKESTOP was a multicentre, parallel group, unmasked, randomised controlled trial done in Halland and Stockholm in Sweden. All 75–76-year-olds residing in these two regions were randomly assigned (1:1) to be invited to screening for atrial fibrillation or to a control group. Participants attended local screening centres and those without a history of atrial fibrillation were asked to register intermittent electrocardiograms (ECGs) for 14 days. Treatment with oral anticoagulants was offered if atrial fibrillation was detected or untreated. All randomly assigned individuals were followed up in the intention-to-treat analysis for a minimum of 5 years for the primary combined endpoint of ischaemic or haemorrhagic stroke, systemic embolism, bleeding leading to hospitalisation, and all-cause death.

## **Findings**

From March 1, 2012, to May 28, 2014, 28 768 individuals were assessed for eligibility and randomly assigned to be invited to screen-

ing (n=14387) or the control group (n=14381). 408 individuals were excluded from the intervention group and 385 were excluded from the control group due to death or migration before invitation. There was no loss to follow-up. Of those invited to screening, 7165 (51.3%) of 13979 participated. After a median follow-up of 6.9 years (IQR 6.5–7.2), significantly fewer primary endpoint events occurred in the intervention group (4456 [31.9%] of 13979; 5.45 events per 100 years [95% CI 5.52–5.61]) than in the control group (4616 [33.0%] of 13996; 5.68 events per 100 years [5.52–5.85]; hazard ratio 0.96 [95% CI 0.92–1.00]; p=0.045).

### Interpretation

Screening for atrial fibrillation showed a small net benefit compared with standard of care, indicating that screening is safe and beneficial in older populations.

## Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study

*Svennberg, E, Engdahl J, Al-Khalili F, Friberg L, Frykman V & Rosenqvist M. Circulation, 2015.*

### 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- to 76-year-old individuals and to study the feasibility of initiating protective oral anticoagulant treatment (OAC).

### Methods and Results

Half of the 75- to 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 95%). 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% 95%) 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.

### Conclusion

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.

## Stepwise Screening of Atrial Fibrillation in a 75-Year Old Population: Implications for Stroke Prevention (StrokeStop pilot)

*Engdahl J, Andersson L, Mirskaya M, Rosenqvist M. Circulation, 2013.*

### Background

Atrial fibrillation (AF) is a frequent source of cardiac emboli in patients with ischemic stroke. AF may be asymptomatic and therefore undiagnosed. Screening for silent AF seems suitable in risk populations, little is however known on the yield and cost-effectiveness of such screening.

## Methods and Results

All inhabitants in the municipality of Halmstad, Sweden age 75-76 were invited to a stepwise screening program for AF. As a first step, participants recorded a 12-lead ECG and reported their relevant medical history. Those with sinus rhythm on 12-lead ECG, no history of AF and at least two risk factors according to CHADS2 were invited to a 2 week recording period using a hand-held ECG asked to record 20 or 30 seconds twice daily and if palpitations occurred. 1330 inhabitants were invited of whom 848 (64%) participated. Previously undiagnosed silent AF was found in 10 (1%) among 848 individuals who recorded 12-lead ECG. Among 81 patients with known AF, 35 (43%) were not on OAC treatment. Among 403 persons with at least two risk factors for stroke, who completed the hand-held ECG event recording, 30 (7.4%) were diagnosed with paroxysmal AF. Thus 75/848 (9%) of the screened population were candidates for new OAC treatment, of those 57 actually started OAC treatment.

## Conclusion

Stepwise risk factor-stratified AF screening in a 75-year old population yields a large share of candidates for OAC treatment on AF indication.

# Uptake of atrial fibrillation screening aiming at stroke prevention: Geomapping of target population and non-participation

*Engdahl J, Holmén A, Rosenqvist M & Strömberg U. BMC Public Health, 2013.*

## Background

In a screening study for silent atrial fibrillation (AF), which is a frequent source of cardiac emboli with ischemic stroke, the proportion of non-participants was considerable and their clinical profile differed

from the participants' profile. We intended to geo-map the target population and non-participation in an attempt to understand factors related to screening uptake and, thereby, obtain useful information needed to intervene for improved uptake.

## Method

In the municipality of Halmstad, Sweden, all residents born in 1934–1935 were invited to the screening study during April 2010 to February 2012. The total study group included 848 participants and 367 non-participants from 12 parishes. Geo-maps displaying participation, along with target-population-based geo-maps displaying proportion of immigrants and ischemic stroke incidence, were used.

## Results

Smoothed non-participation ratios (SmNPR) varied from 0.81 to 1.24 across different parishes (SmNPR = 1 corresponds to the expected participation based on the total study group). Among high risk individuals, the geographical variation was more pronounced (SmNPR range 0.75–1.51). Two parishes with higher share of immigrants and elevated population-based ischemic stroke incidence showed markedly lower participation, particularly among high-risk individuals.

## Conclusion

AF screening uptake varied evidently between parishes, particularly among high-risk individuals. Geo-mapping of target population and non-participation yielded useful information needed to intervene for improved screening uptake.

# A prospective 5-year follow-up after population based systematic screening for atrial fibrillation

*Engdahl J, Holmén A, Rosenqvist M, Strömberg U. Europace, 2018.*

## **Aims**

Thrombo-embolic stroke risk in atrial fibrillation (AF) is significantly reduced with oral anticoagulant (OAC) treatment. Atrial fibrillation is often asymptomatic (silent) and therefore undiagnosed. The long-term course of silent AF as well as OAC treatment adherence after AF screening is not known. We aim at studying long-term adherence to OAC treatment, AF symptoms, and stroke incidence on population level after systematic AF screening.

## **Methods and results**

All inhabitants in a Swedish municipality who were born in 1934 and 1935 (n = 1335) were invited to participate in an AF screening trial between 2010 and 2012. Participants with a previously known or screening-detected AF were invited to a 5-year follow-up. Time trends of ischaemic stroke incidence were compared for population groups residing in the intervention municipality and in a surrounding control area where no AF screening trial was carried out. After the screening procedure, 103 of 121 participants (85%) with AF were treated with OAC. At the follow-up examination, 94 of 106 living patients (88%) were still on OAC treatment. Among the 23 long-term surviving patients who were diagnosed with paroxysmal AF during screening, 6 had developed permanent silent AF. The incidence of ischaemic stroke between ages 76–80 years declined significantly after the AF screening trial in the intervention area (P = 0.003) but not in the control area.

## **Conclusion**

Adherence to OAC treatment 5 years after AF screening was high. Silent AF has a natural course similar to symptomatic AF. The observed incidences of ischaemic stroke suggest a beneficial population-level effect of systematic AF screening.

# Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: The STROKESTOP II study

*Gudmundsdottir K K, Fredriksson T, Svennberg E, Al-Khalili F, Friberg L, Frykman V, Hijazi Z, Rosenqvist M & Engdahl J. Europace, 2019.*

## Aims

To study the prevalence of unknown atrial fibrillation (AF) in a high-risk population (75/76-year old) using N-terminal B-type natriuretic peptide (NT-proBNP) and handheld electrocardiogram (ECG) recordings in a stepwise screening procedure.

## Methods and Results

The STROKESTOP II study is a population-based cohort study in which all 75/76-year-old in the Stockholm region (n=28 712) were randomized 1:1 to be invited to an AF screening programme or to serve as the control group. Participants without known AF had NT-proBNP analysed and were stratified into low-risk (NT-proBNP<125ng/L) and high-risk (NT-proBNP>125 ng/L) groups. The high-risk group was offered extended ECG-screening, whereas the low-risk group performed only one single lead ECG recording. In total, 6868 individuals accepted the screening invitation of which 6315 (91.9%) did not have previously known AF. New AF was detected in 2.6% (5% confidence interval (CI) 2.2-3.0) of all participants without previous AF. In the high-risk group (n=3766/6315, 59.6%), AF was diagnosed in 4.4% (95% CI 3.7-5.1) of the participants. Out of these, 18% had AF on their index-ECG. In the low-risk group, one participant was diagnosed with AF on index-ECG. The screening procedure resulted in an increase in known prevalence from 8.1% to 10.5% among participants. Oral anticoagulation treatment was initiated in 94.5% of the participants with newly diagnosed AF.



## Conclusion

N-terminal B-type natriuretic peptide-stratified systematic screening for AF identified 4.4% of the high-risk participants with new AF oral anticoagulant treatment initiation was well accepted in the group diagnosed with new AF.

# Screening for atrial fibrillation with baseline and intermittent ECG recording in an out-of-hospital population (FLIP)

*Hendrikx T, Hörnsten R, Rosenqvist M, Sandström H. BMC Cardiovascular Disorders, 2013.*

## Background

The objective of this study is to investigate the detection rate of undiagnosed atrial fibrillation (AF) with short intermittent ECG recordings during four weeks among out-of-hospital patients, having at least one additional risk factor (CHADS<sub>2</sub>) for stroke.

## Method

Design: Cross-sectional study. Setting: Eight family practice centres and two hospital-based out-patient clinics in Sweden. Subjects: 989 out-of-hospital patients, without known AF, having one or more risk factors associated with stroke (CHADS<sub>2</sub>). Interventions: All individuals were asked to perform 10-second handheld ECG recordings during 28 days, twice daily and when having palpitations. Main outcome measures: Episodes of AF on handheld ECG recordings were defined as irregular supraventricular extrasystoles in series with a duration of 10 seconds.

## Results

928 patients completed registration. AF was found in 35 of 928 patients; 3.8% (95% confidence interval [CI] 2.7–5.2). These 35 patients

had a mean age of 70.7 years (SD  $\pm$  7.7; range 53–85) and a median CHADS2 of 2 (range 1–4).

### Conclusion

Intermittent handheld ECG recording over a four week period had a detection rate of 3.8% newly diagnosed AF, in a population of 928 out-of-hospital patients having at least one additional risk factor for stroke. Intermittent handheld ECG registration is a feasible method to detect AF in patients with an increased risk of stroke in whom oral anticoagulation (OAC) treatment is indicated.

## Systematic screening for atrial fibrillation in a 65-year-old population with risk factors for stroke: Data from the Akershus Cardiac Examination 1950 study

*Berge T, Brynildsen J, Larssen HKN, Onarheim S, Jenssen GR, Ihle-Hansen H, Christophersen IE, Myrstad M, Røsjø H, Smith, P & Tveit A. *Europace*, 2017.*

### Aims

To investigate the yield of screening for atrial fibrillation (AF) in a cohort of 65-year-old individuals from the general population with additional risk factors for stroke.

### Methods and results

We invited participants with additional risk factors for stroke (CHA2DS2-VASc score  $\geq$  2 for men or  $\geq$  3 for women) without previously known AF from a population-based study in Norway to participate in a 2-week screening for AF. Screening was performed by one-lead 'thumb electrocardiography (ECG)' recordings of 30s twice daily or

when the participants experienced symptoms. In total, 1742 (47.0%) participants of the Akershus Cardiac Examination (ACE) 1950 study had at least one additional risk factor for stroke. Of these, 123 cases reported a history of AF and 101 (5.8%) cases were ECG validated. Eight [0.5%, 95% confidence interval (CI) 0.2-0.9] new AF cases were diagnosed by 12-lead ECG at baseline, and 10 additional participants were diagnosed with AF before screening commenced. We invited all 1601 participants who met the inclusion criteria for screening, of which 1510 (94.3%) participants were included (44% women and 56% men). The screening revealed AF in 13 (0.9%, 95% CI 0.5-1.5) participants. The total prevalence of ECG-validated AF after screening among the 65-year-olds with risk factors for stroke was 7.6% (95% CI 6.4-8.9), in men 10.0% (95% CI 8.2-12.0), and in women 4.3% (95% CI 3.0-6.1) ( $P < 0.001$ ).

### Conclusion

In a group of 1510 well-characterized 65-year-olds with risk factors for stroke, 2-week intermittent ECG screening identified undiagnosed AF in 0.9%. The total prevalence of AF was 7.6%.

## Feasibility and outcomes of atrial fibrillation screening using intermittent electrocardiography in a primary healthcare setting: A cross-sectional study

*Ghazal F, Theobald H, Rosenqvist M, Al-Khalili F. PLOS One, 2018.*

### Background

Atrial fibrillation (AF) is a major risk factor for ischemic stroke unless treated with an anticoagulant. Detecting AF can be difficult because AF is often paroxysmal and asymptomatic. The aims of this study were

to develop a screening model to detect AF in a primary healthcare setting and to initiate oral anticoagulant therapy in high-risk patients to prevent stroke.

## Methods

This was a cross-sectional study. All 70- to 74-year-old individuals registered at a single primary healthcare center in Stockholm were invited to participate in AF screening upon visiting the center during a ten-month period. Those who did not have contact with the center during this period were invited to participate by letter. Thirty-second intermittent ECG recordings were made twice a day using a handheld Zenicor device over a 2-week period in participants without AF. Oral anticoagulant therapy was offered to patients with newly detected AF.

## Findings

Of the 415 eligible individuals, a total of 324 (78.1%) patients participated in the study. The mean age of the participants was 72 years, 52.2% were female, and the median CHA<sub>2</sub>DS<sub>2</sub>-VASc score of the participants was 3. In the target population, 34 (8.2%) individuals had previously diagnosed AF. Among participants without previously known AF, 16 (5.5%) cases of AF were detected. The final AF prevalence in the target population was 12%. Oral anticoagulant therapy was successfully initiated in 88% of these patients with newly detected AF.

## Conclusions

The AF screening project exhibited a high participation rate and resulted in a high rate of newly discovered AF; of these newly diagnosed patients, 88% could be treated with an oral anticoagulant.

# ECG Interpretation

# Sensitivity and specificity of handheld one lead ECG detecting atrial fibrillation in an outpatient clinic setting

*Malmqvist, J., Engdahl, J., Sjölund, G., & Doliwa, P. (2024)*

## **Abstract/Aims**

To validate the sensitivity and specificity of the Zenicor One handheld ECG device for detection of atrial fibrillation in an outpatient clinical setting.

## **Methods and results**

Patients attending outpatient clinics at Danderyd Hospital (n = 220) were examined with one lead handheld ECG immediately after standard care 12-lead ECG recording. Twelve recordings were excluded (atrial flutter or pacing) or missing. The recordings were dichotomously categorized as "atrial fibrillation" or "not atrial fibrillation" by two senior cardiologists. In cases of diverging interpretations, a third senior cardiologist had the deciding vote. Sensitivity and specificity in diagnosing atrial fibrillation was calculated with 12-lead ECG as gold standard. Sensitivity and specificity for diagnosis of atrial fibrillation with one lead handheld ECG and 12-lead ECG as gold standard was 98% and 99% respectively.

## **Conclusion**

In a health-care outpatient setting, Zenicor One handheld ECG had high sensitivity and specificity for detection of atrial fibrillation when compared with 12-lead ECG.

# Short-term ECG for out of hospital detection of silent atrial fibrillation episodes

*Sobosinski Doliwa P, Frykman V & Rosenqvist M. Scand Cardiovascular J, 2009.*

## Objectives

We evaluated a short-term ECG, thumb ECG, for detection of asymptomatic atrial fibrillation (AF) episodes. The aim was to evaluate registration efficacy, sensitivity, specificity, quality and feasibility in patients with special emphasis on asymptomatic AF.

## Design

One hundred patients registered their cardiac rhythm with 12-lead ECG immediately followed by thumb ECG. The registrations were compared blindly. A second group of 12 patients, who had successfully undergone cardioversion, performed rhythm registration twice daily for 30 days. A third group of 606 individuals underwent an AF screening procedure.

## Results

Thumb ECG correctly diagnosed AF (sensitivity) in 96% and sinus rhythm (specificity) in 92% compared with 12-lead ECG. In the group of cardioverted patients, 466 registrations were validated: 95% had satisfactory quality for diagnosis: four patients experienced AF recurrence in which three were asymptomatic. In the third group 12 persons were diagnosed with AF, six of these had neither symptoms nor a history of AF.

## Conclusions

Short-term ECG is able to diagnose AF with a high sensitivity, specificity and simple application making detection of asymptomatic AF possible for screening purposes.

# Safe automatic one-lead electrocardiogram analysis in screening for atrial fibrillation

*Svennberg E, Stridh M, Engdahl J, Al-Khalili F, Friberg L, Frykman V & Rosenqvist M. Europace, 2016.*

## Aims

Screening for atrial fibrillation (AF) using intermittent electrocardiogram (ECG) recordings can identify individuals at risk of AF-related morbidity in particular stroke. We aimed to validate the performance of an AF screening algorithm compared with manual ECG analysis by specially trained nurses and physicians (gold standard) in 30 s intermittent one-lead ECG recordings.

## Methods and Results

The STROKESTOP study is a mass-screening study for AF using intermittent ECG recordings. All individuals in the study without known AF registered a 30-s ECG recording in Lead I two times daily for 2 weeks, and all ECGs were manually interpreted. A computerized algorithm was used to analyse 80 149 ECG recordings in 3209 individuals. The computerized algorithm annotated 87.1% (n = 69 789) of the recordings as sinus rhythm/minor rhythm disturbances. The manual interpretation (gold standard) was that 69 758 ECGs were normal, making the negative predictive value of the algorithm 99.9%. The number of ECGs requiring manual interpretation in order to find one pathological ECG was reduced from 288 to 35. Atrial fibrillation was diagnosed in 84 patients by manual interpretation, in all of whom the algorithm indicated pathology. On an ECG level, 278 ECGs were manually interpreted as AF, and of these the algorithm annotated 272 ECGs as pathological (sensitivity 97.8%).

## Conclusion

Automatic ECG screening using a computerized algorithm safely identifies normal ECGs in Lead I and reduces the need for manual evaluation of individual ECGs with >85% with 100% sensitivity on an individual basis.



# Screening for Atrial Fibrillation: Improving Efficiency of Manual Review of Handheld Electro- cardiograms

*Pandiaraja M, Brimicombe J, Cowie M, Dymond A, Clair Lindén H, Lip G, Mant J, Williams K & Charlton PH, 2020.*

## Background

Atrial fibrillation (AF) is a common irregular heart rhythm associated with a five-fold increase in stroke risk. It is often not recognised as it can occur intermittently and without symptoms. A promising approach to detect AF is to use a handheld electrocardiogram (ECG) sensor for screening. However, the ECG recordings must be manually reviewed, which is time-consuming and costly.

## Aims

Our aims were to: (i) evaluate the manual review workload; and (ii) evaluate strategies to reduce the workload.

## Methods and Results

In total, 2141 older adults were asked to record their ECG four times per day for 1-4 weeks in the SAFER (Screening for Atrial Fibrillation with ECG to Reduce stroke) Feasibility Study, producing 162,515 recordings. Patients with AF were identified by: (i) an algorithm classifying recordings based on signal quality (high or low) and heart rhythm; (ii) a nurse reviewing recordings to correct algorithm misclassifications; and (iii) two cardiologists independently reviewing recordings from patients with any evidence of rhythm abnormality. It was estimated that 30,165 reviews were required (20,155 by the nurse, and 5005 by each cardiologist). The total number of reviews could be reduced to 24,561 if low-quality recordings were excluded from review; 18,573 by only reviewing ECGs falling under certain pathological classifications; and 18,144 by only reviewing ECGs displaying an irregularly irregular

rhythm for the entire recording. The number of AF patients identified would not fall considerably: from 54 to 54, 54 and 53, respectively.

### **Conclusion**

In conclusion, simple approaches may help feasibly reduce the manual workload by 38.4% whilst still identifying the same number of patients with undiagnosed, clinically relevant AF.

# Data-driven **screening**

# Future Innovations in Novel Detection for Atrial Fibrillation (FIND-AF): pilot study of an electronic health record machine learning algorithm guided intervention to identify undiagnosed atrial fibrillation

*Nadarajah R, Wahab A, Reynolds C, Raveendra K, Askham D, Dawson R, Keene J, Shanghavi S, Lip G Y H, Hogg D, Cowan C, Wu J & Gale C P. 2023.*

## **Introduction**

Atrial fibrillation (AF) is associated with a fivefold increased risk of stroke. Oral anticoagulation reduces the risk of stroke, but AF is elusive. A machine learning algorithm (Future Innovations in Novel Detection of Atrial Fibrillation (FIND-AF)) developed to predict incident AF within 6 months using data in primary care electronic health records (EHRs) could be used to guide AF screening. The objectives of the FIND-AF pilot study are to determine yields of AF during ECG monitoring across AF risk estimates and establish rates of recruitment and protocol adherence in a remote AF screening pathway.

## **Methods and analysis**

The FIND-AF Pilot is an interventional, non-randomised, single-arm, open-label study that will recruit 1955 participants aged 30 years or older, without a history of AF and eligible for oral anticoagulation, identified as higher risk and lower risk by the FIND-AF risk score from their primary care EHRs, to a period of remote ECG monitoring with a Zenicor-ECG device. The primary outcome is AF diagnosis during ECG mo-

monitoring, and secondary outcomes include recruitment rates, withdrawal rates, adherence to ECG monitoring and prescription of oral anticoagulation to participants diagnosed with AF during ECG monitoring.

### **Ethics and dissemination**

The study has ethical approval (the North West-Greater Manchester South Research Ethics Committee reference 23/NW/0180). Findings will be announced at relevant conferences and published in peer-reviewed journals in line with the Funder's open access policy.

# **An artificial intelligence based-model for prediction of atrial fibrillation from single-lead sinus rhythm electrocardiograms facilitating screening**

*Hygrell T, Viberg F, Dahlberg E, Charlton P H, Kemp Gudmundsdottir K, Mant J, Lindman Hörnlund J, Svennberg E. 2023.*

### **Abstract Aims**

Screening for atrial fibrillation (AF) is recommended in the European Society of Cardiology guidelines. Yields of detection can be low due to the paroxysmal nature of the disease. Prolonged heart rhythm monitoring might be needed to increase yield but can be cumbersome and expensive. The aim of this study was to observe the accuracy of an artificial intelligence (AI)-based network to predict paroxysmal AF from a normal sinus rhythm single-lead ECG.

### **Methods and results**

A convolutional neural network model was trained and evaluated using data from three AF screening studies. A total of 478 963 single-lead

ECGs from 14 831 patients aged  $\geq 65$  years were included in the analysis. The training set included ECGs from 80% of participants in SAFER and STROKESTOP II. The remaining ECGs from 20% of participants in SAFER and STROKESTOP II together with all participants in STROKESTOP I were included in the test set. The accuracy was estimated using the area under the receiver operating characteristic curve (AUC). From a single timepoint ECG, the artificial intelligence-based algorithm predicted paroxysmal AF in the SAFER study with an AUC of 0.80 [confidence interval (CI) 0.78-0.83], which had a wide age range of 65-90+ years. Performance was lower in the age-homogenous groups in STROKESTOP I and STROKESTOP II (age range: 75-76 years), with AUCs of 0.62 (CI 0.61-0.64) and 0.62 (CI 0.58-0.65), respectively.

### **Conclusion**

An artificial intelligence-enabled network has the ability to predict AF from a sinus rhythm single-lead ECG. Performance improves with a wider age distribution.

Cost-effectiveness  
**Secondary and  
primary stroke  
prevention**

# Cost-effectiveness of population screening for atrial fibrillation: the STROKESTOP study

*Lyth J, Svennberg E, Bernfort L, Aronsson M, Frykman V, Al-Khalili F, Friberg L, Rosenqvist M, Engdahl J, Levin L-Å. European Heart J, 2023.*

## **Abstract**

Aims: Previous studies on the cost-effectiveness of screening for atrial fibrillation (AF) are based on assumptions of long-term clinical effects. The STROKESTOP study, which randomised 27 975 persons aged 75/76 years into a screening invitation group and a control group, has a median follow-up time of 6.9 years. The aim of this study was to estimate the cost-effectiveness of population-based screening for AF using clinical outcomes.

## **Methods and results**

The analysis is based on a Markov cohort model. The prevalence of AF, the use of oral anticoagulation, clinical event data, and all-cause mortality were taken from the STROKESTOP study. The cost for clinical events, age-specific utilities, utility decrement due to stroke, and stroke death was taken from the literature. Uncertainty in the model was considered in a probabilistic sensitivity analysis. Per 1000 individuals invited to the screening, there were 77 gained life years and 65 gained quality-adjusted life years. The incremental cost was €1.77 million lower in the screening invitation group. Gained quality-adjusted life years to a lower cost means that the screening strategy was dominant. The result from 10 000 Monte Carlo simulations showed that the AF screening strategy was cost-effective in 99.2% and cost-saving in 92.7% of the simulations. In the base-case scenario, screening of 1000 individuals resulted in 10.6 [95% confidence interval (CI): -22.5 to 1.4] fewer strokes (8.4 ischaemic and 2.2 haemorrhagic strokes), 1.0 (95% CI: -1.9 to 4.1) more cases of systemic embolism, and 2.9 (95% CI: -18.2 to 13.1) fewer bleedings associated with hospitalization.



## Conclusion

Based on the STROKESTOP study, this analysis shows that a broad AF screening strategy in an elderly population is cost-effective. Efforts should be made to increase screening participation.

# Cost-effectiveness of screening for atrial fibrillation in a single primary care center at a 3-year follow-up

*Ghazal F, Aronsson M, Al-Khalili F, Rosenqvist M & Levin L-Å. 2022.*

## Objectives

The aim of this study was to estimate the cost-effectiveness of intermittent electrocardiogram (ECG) screening for atrial fibrillation (AF) among 70–74-year old individuals in primary care. We also aimed to assess adherence to anticoagulants, severe bleeding, stroke and mortality among screening-detected AF cases at three-year follow-up.

## Methods

A post hoc analysis based on a cross-sectional screening study for AF among 70–74-year old patients, who were registered at a single primary care center, was followed for three years for mortality. Data about adherence to anticoagulants, incidence of stroke and severe bleeding among screening-detected AF cases, were collected from patient's records. Markov model and Monte Carlo simulation were used to assess the cost-effectiveness of the screening program.

## Results

The mortality rate among screening-detected AF cases ( $n = 16$ ) did not differ compared to the 274 individuals with no AF (hazard ratio 0.86, CI 0.12–6.44). Adherence to anticoagulants was 92%. There was no stroke or severe bleeding. The incremental cost-effectiveness ratio

of screening versus no screening was EUR 2389/quality-adjusted life year (QALY) gained. The screening showed a 99% probability of being cost-effective compared to no screening at a willingness-to-pay threshold of EUR 20,000 per QALY.

### **Conclusion**

Screening for AF among 70–74-year-olds in primary care using intermittent ECG appears to be cost-effective at 3-year follow-up with high anticoagulants adherence and no increased mortality.

## **A cost-effectiveness analysis of screening for silent atrial fibrillation after ischaemic stroke**

*Levin L, Husberg M, Doliwa Sobocinski P, Frykman Kull V, Friberg L, Rosenqvist M & Davidson T. *Europace*, 2014.*

### **Aims**

The purpose of this study was to estimate the cost-effectiveness of two screening methods for detection of silent AF, intermittent electrocardiogram (ECG) recordings using a handheld recording device, at regular time intervals for 30 days, and short-term 24 h continuous Holter ECG, in comparison with a no-screening alternative in 75-year-old patients with a recent ischaemic stroke.

### **Methods and Results**

The long-term (20-year) costs and effects of all alternatives were estimated with a decision analytic model combining the result of a clinical study and epidemiological data from Sweden. The structure of a cost-effectiveness analysis was used in this study. The short-term decision tree model analysed the screening procedure until the onset of anticoagulant treatment. The second part of the decision model followed a Markov design, simulating the patients' health states for 20 years. Continuous 24 h ECG recording was inferior to intermittent ECG

in terms of cost-effectiveness, due to both lower sensitivity and higher costs. The base-case analysis compared intermittent ECG screening with no screening of patients with recent stroke. The implementation of the screening programme on 1000 patients resulted over a 20-year period in 11 avoided strokes and the gain of 29 life-years, or 23 quality-adjusted life years, and cost savings of €55 400.

### **Conclusion**

Screening of silent AF by intermittent ECG recordings in patients with a recent ischaemic stroke is a cost-effective use of health care resources saving costs and lives and improving the quality of life.

## **Assessment Regarding Primary Preventive Screening of Atrial Fibrillation with Thumb ECG**

*Tandvårds- och läkemedelsförmånsverket, 2014.*

The Swedish Dental and Pharmaceutical Benefits Agency (TLV) has performed an economic evaluation of the method primary preventive screening of atrial fibrillation (AF) with thumb ECG. Thumb ECG is a mobile device for ECG recordings and TLV concludes that the use of the method is reasonably cost-effective according to available data.

### **TLV's commission on medical devices**

TLV has been commissioned by the Government to conduct health technology assessments of medical devices in an early stage of the product life cycle. The commission was initiated to aid the county councils in making more informed decisions. The county councils have also expressed a need for the assessments to contain aspects such as ethical considerations, legal aspects, organisational consequences and environmental issues. Another goal was to perform economic evaluations at the national level, previously not done in Sweden, which enables uniformity and equal health care. The present evaluation constitutes a

part of the commission and has been conducted on a trial basis during the last three years.

Despite limited available scientific data, TLV considers that it is possible to evaluate medical devices at an early stage of the product life cycle, based on the same methods as for pharmaceuticals. A final report has been submitted at the end of December 2014. The Government has commissioned TLV to continue evaluating medical devices at an early stage of the product life cycle throughout the year 2015.

## Introduction

Every year approximately 25,000 cases of acute stroke are registered. Approximately 20 per cent of all ischaemic strokes are caused by AF. Stroke is the most common cause of chronic functional impairments among adults and results in considerable health care needs. If AF is detected medical treatment with anticoagulants can be initiated, with the aim to prevent future strokes. Thumb ECG is a CE marked medical device still in an early stage in the product life cycle.

Thumb ECG is a mobile device for ECG recordings used for population screening for AF outside health care services. This method allows the individual to register his/ her ECG data at home by pressing a button and placing their thumbs on the device for approximately 30 seconds. It can be used over an extended period (e.g. twice daily over a period of two or four weeks). The results are electronically transmitted to the health care provider.

## The STROKESTOP study

Primary prevention screening of AF has not previously been studied in a clinical study. The STROKESTOP study is an ongoing clinical study in two county councils in Sweden. The aim of the study was to find individuals with AF and to be able to treat these preventatively with anticoagulants to avoid stroke.

All persons born in 1936 and 1937 in the studied county councils were identified and by means of randomisation invited to participate in the screening programme or in the control arm. Approximately 13,000 persons were approached for inclusion in the screening programme and approximately 7,000 persons participated. TLV has used the preliminary results from the STROKESTOP study in the cost-effectiveness analysis in this assessment.

## **Aim of the assessment**

The purpose of this assessment was to study whether the method of primary preventive screening of AF with thumb ECG is cost-effective for 75 year old individuals.

## **Uncertainty regarding the number of detected atrial fibrillation**

The AF detection rate used in this economic evaluation is based on the ongoing clinical STROKESTOP study. The clinical study shows that primary preventive screening results in both earlier and higher detection rate of AF compared to routine health care.

An economic evaluation is always associated with a certain degree of uncertainty. The scientific evidence base for medical devices is usually less comprehensive than for pharmaceuticals. The uncertainty in this case is largely related to the number of AF cases detected during screening. There is considerably less uncertainty regarding whether the stroke prevention treatment is cost-effective for those diagnosed with AF.

## **Primary preventive screening is cost-effective**

The assessment shows that the cost of primary preventive screening with thumb ECG is approximately SEK 39,000 per quality-adjusted life-year (QALY) gained.

TLV has also analysed how the budgets of county councils and municipalities will be affected if screening with thumb ECG is introduced for individuals aged 75.

In Sweden, the county councils are responsible for specialised care, in this case acute stroke care. The municipalities, on the other hand, are responsible for rehabilitation of stroke patients. For county councils it will result in higher costs due to the introduction of the screening programme. However, the costs will be offset as the numbers of strokes will decline as a result of the screening programme. The costs for municipalities will decrease as the number of stroke patients are expected to decline. Avoiding stroke will not only result in health benefits for the patients, but also decreased health care costs related to stroke for the society.

TLV concludes that the benefits of primary preventive screening with thumb ECG seem large enough to justify the costs of screening for the studied population. This evaluation is based on the best available knowledge and might change in the future.

### Follow-up and evaluation

There is currently no information regarding when to initiate a national screening programme i.e. at which cut-off age the method becomes cost-effective. TLV have the intention to evaluate this in a separate report in the future.

## Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording

*Aronsson M, Svennberg E, Rosenqvist M, Engdahl J, Al-Khalili F, Friberg L, Frykman-Kull V & Levin L-Å. Europace, 2015.*

### Aims

The aim of this study was to estimate the cost-effectiveness of 2 weeks of intermittent screening for asymptomatic atrial fibrillation (AF) in 75/76-year-old individuals.

### Methods and Results

The cost-effectiveness analysis of screening in 75-year-old individuals was based on a lifelong decision analytic Markov model. In this model, 1000 hypothetical individuals, who matched the population of the STROKESTOP study, were simulated. The population was analysed for different parameters such as prevalence, AF status, treatment with oral anticoagulation, stroke risk, utility, and costs. In the base-case scenario, screening of 1000 individuals resulted in 263 fewer patient-years with undetected AF. This implies eight fewer strokes, 11 more life-years, and 12 more quality-adjusted life years (QALYs) per 1000 screened individuals. The screening implies an incremental cost of €50 012, resulting in a cost of €4313 per gained QALY and €6583 per avoided stroke.

## Conclusion

With the use of a decision analytic simulation model, it has been shown that screening for asymptomatic AF in 75/76-year-old individuals is cost-effective.



# Complete list of published research

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6. **Berge, T., Brynildsen, J., Larssen, H. K. N., Onarheim, S., Jenssen, G. R., Ihle-Hansen, H., Christophersen, I. E., Myrstad, M., Røsjø, H., Smith, P., & Tveit, A.** (2018). Systematic screening for atrial fibrillation in a 65-year-old population with risk factors for stroke: data from the Akershus Cardiac Examination 1950 study. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*, 20(FI\_3), f299–f305.  
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**Zenicor Medical Systems AB**  
Saltmätargatan 8  
113 59 Stockholm  
+46-8-442 68 60  
[www.zenicor.se](http://www.zenicor.se)  
[info@zenicor.com](mailto:info@zenicor.com)

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