

# The importance and future of population screening for atrial fibrillation

Shin, Seung Yong; Lip, Gregory

DOI:

[10.1016/j.cjca.2018.08.016](https://doi.org/10.1016/j.cjca.2018.08.016)

License:

Creative Commons: Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

*Document Version*

Peer reviewed version

*Citation for published version (Harvard):*

Shin, SY & Lip, G 2018, 'The importance and future of population screening for atrial fibrillation', *Canadian Journal of Cardiology*. <https://doi.org/10.1016/j.cjca.2018.08.016>

[Link to publication on Research at Birmingham portal](#)

## General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

## Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact [UBIRA@lists.bham.ac.uk](mailto:UBIRA@lists.bham.ac.uk) providing details and we will remove access to the work immediately and investigate.

# Accepted Manuscript



The importance and future of population screening for atrial fibrillation

Seung Yong Shin, MD, Gregory Y.H. Lip, MD, Professor

PII: S0828-282X(18)31051-1

DOI: [10.1016/j.cjca.2018.08.016](https://doi.org/10.1016/j.cjca.2018.08.016)

Reference: CJCA 3015

To appear in: *Canadian Journal of Cardiology*

Received Date: 7 May 2018

Revised Date: 9 August 2018

Accepted Date: 9 August 2018

Please cite this article as: Shin SY, Lip GYH, The importance and future of population screening for atrial fibrillation, *Canadian Journal of Cardiology* (2018), doi: 10.1016/j.cjca.2018.08.016.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**The importance and future of population screening for atrial fibrillation**

Seung Yong Shin, MD<sup>1,2</sup>

Gregory Y.H. Lip, MD.<sup>1,3</sup>

<sup>1</sup> Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, United Kingdom

<sup>2</sup> Cardiovascular & Arrhythmia Center, Chung-Ang University Hospital, Chung-Ang University, Seoul, Republic of Korea

<sup>3</sup> Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart and Chest Hospital, Liverpool, United Kingdom

**Correspondence:**

Professor G.Y.H. Lip,

Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, UK

Tel: +44 121 507 5080; E-mail: [G.Y.H.Lip@bham.ac.uk](mailto:G.Y.H.Lip@bham.ac.uk)

**Brief summary**

Atrial fibrillation is known as one of major causes of increased cardiovascular mortality and ischemic stroke. Especially at the preclinical stage, the potential benefit of appropriate screening and preventive intervention to patients with increased stroke risk may be expected. In this review article, we will discuss the importance and future perspectives of population screening for atrial fibrillation.

**Abstract**

Atrial fibrillation (AF) is a common and progressive heart rhythm disorder that causes structural, functional and electrical remodelling of the heart. Although we do not fully understand AF yet, this arrhythmia is one clinical feature of a syndrome that is represented by irregularly irregular atrial rhythm accompanied by progressive atrial structural and functional remodelling. Although ischemic stroke, most feared complication of AF, can be prevented by anticoagulation, asymptomatic or paroxysmal nature of AF makes timely diagnosis of AF difficult. Thus, appropriate screening method for AF is necessary. In this review, we will discuss the importance and future perspectives of population screening for AF.

## Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and its global prevalence is increasing<sup>1, 2</sup>. Serious subsequent complications such as ischemic stroke, deterioration of heart function, increased mortality, and impaired quality of life are medically important problems with social and public health implications<sup>1-5</sup>.

Indeed, in patients with clinically diagnosed AF, appropriate stroke prevention is possible, but only if AF is detected prior to ischemic stroke onset<sup>6</sup>. Unfortunately, stroke can be the first presentation of AF, which can be a double problem, given that AF-associated strokes are associated with a worse prognosis (more often fatal or disabling) compared to non-AF associated strokes. As such, the early identification of patients at high risk of AF-associated strokes, and the initiation of stroke-prevention therapies can be critical<sup>7, 8</sup>.

In this review, we will discuss the importance and future perspectives of population screening for AF.

## Observations on AF associated stroke

AF related strokes are generally thromboembolic, but it is impossible to fully explain all strokes associated with AF as being associated with blood stasis during AF episodes. An analysis of the temporal relationship between the time of stroke onset and AF events recorded in cardiac implanted electric devices (CIEDs) reveals that only 8–30% of patients have AF detected in 30 days before the stroke onset and up to 15% of patients have AF detected only after stroke onset<sup>9-11</sup>. Regardless of the temporal association between AF episode and stroke onset, device-detected AF results in a ~2.5 fold increased stroke risk, the necessity of

anticoagulation might be carefully determined where stroke risk factors are present<sup>12-14</sup>.

In the classification of ischemic stroke, Trial of Org 10172 in Acute Stroke Treatment classification is widely used and denotes five subtypes of ischemic stroke: (i) large-artery atherosclerosis, (ii) cardio-embolism, (iii) small-vessel occlusion, (iv) stroke of other determined aetiology, and (v) stroke of undetermined etiology<sup>15</sup>. Cryptogenic stroke, or known as Embolic Strokes of Undetermined Source (ESUS), are defined as: (i) non-lacunar brain infarct on imaging, (ii) <50% arterial stenosis proximal to the infarct, and (iii) no major-risk cardio-embolic source (including no permanent or paroxysmal atrial fibrillation diagnosed by ECG)<sup>16</sup>. ESUS comprises about 1 in 6 ischemic strokes<sup>17</sup>. Since recurrence rate of stroke is substantial (4.5% per year) during (mostly) antiplatelet therapy, clear identification of its pathogenesis and appropriate anti-thrombotic management are necessary. Because subclinical AF (SCAF) may play an important role in the pathogenesis of cardio-embolic stroke corresponding to ESUS, screening for SCAF with accuracy and efficacy is necessary, and that subsequent intervention of SCAF shows net benefit.<sup>18</sup>

Since SCAF can be documented in CIEDs, studies of AF detection in patients with CIEDs have demonstrated that the incidence of SCAF varies greatly (28–68%) depending on the clinical profile of enrolled patients, follow-up duration, and applied diagnostic criteria<sup>18-22</sup>. Despite the different diagnostic criteria and follow-up periods between studies, all patients with SCAF documented in CIEDs showed a 2.1–6.7 fold increase in stroke risk<sup>12, 18, 20, 23-26</sup>. Therefore, patients with CIEDs and SCAF may benefit from close follow-up and risk stratification<sup>18</sup>. For those with SCAF duration  $\geq 24$  hours, there is likely a benefit from anticoagulation<sup>27</sup>. In those patients with SCAF duration < 24 hours and clinical risk factors, ongoing randomized trials will answer definitively whether anticoagulation of SCAF

documented in CIEDs can reduce ischemic stroke and systemic embolism (ARTESiA trial: NCT01938248, NOAH trial: NCT02618577)<sup>28, 29</sup>.

However, in the absence of CIEDs, such prolonged continuous monitoring is not readily available. Therefore, different screening methods are recommended to meet the clinical needs of individual patients, such as automated blood pressure monitoring<sup>30, 31</sup>, ECG or pulse taking in patients' age > 65 years<sup>32-35</sup>, or short-term ECG recording followed by continuous ECG monitoring for at least 72 hours in stroke survivors<sup>36, 37</sup>.

### **Wider population screening for AF**

Although natural history and clinical significance of SCAF is not fully clarified, screening for SCAF by imaging may be justified by the fact that the development of atrial substrate precedes the clinical onset of AF. Furthermore, imaging-based screening may be relevant in providing information regarding the potential risk for SCAF amongst ESUS patients during follow-up. Thus far, it is not clear whether earlier detection of SCAF at this pre-clinical stage is possible or whether treatment would be beneficial. Therefore, more evidence through well-designed studies are needed.

Generally, there are mainly two different types of screening as follows<sup>38</sup>: (i) Opportunistic approach, where targeted patients are screened on appearance once at a single time point measurement, for example, when attending for blood pressure checks, and (ii) Systematic approach, whereby general random patients are invited for screening.

Opportunistic screening allows us to target high risk patient populations that are at risk of incident AF<sup>39</sup>. The first randomised comparison of opportunistic versus systematic screening

for AF was the SAFE (Screening for AF in the Elderly) study, which showed that opportunistic screening was cost-effective at a cost of £562 per additional case of AF detected<sup>34, 40</sup>.

As specific screening methods, pulse palpation or automated blood pressure monitoring (BPM) have been undertaken and these demonstrate good diagnostic yields in a recent meta-analysis (pulse palpation: c-index = 0.93 [95% CI: 0.91–0.95]; BPM: c-index = 0.98 [95% CI: 0.96–0.99])<sup>30, 31, 35</sup>. Furthermore, we are now in the era when new technologies are available that can easily screen for AF. In the SEARCH-AF study, 1,000 participants ( $\geq 65$  years) were screened with smartphone-based automated algorithm, which showed good sensitivity (98.5 %, CI 92 – 100 %) and specificity (91.4 % (CI 89 – 93 %))<sup>41</sup>. The REHEARSE-AF study using portable ECG monitors (AliveCor Kardia) with remote ECG interpretation demonstrated higher incidence of AF compared to routine care (hazard ratio 3.9; 95% CI 1.4–10.4,  $P = 0.007$ ) at a cost per AF diagnosis of \$10780<sup>42</sup>. In a more contemporary example of opportunistic screening for AF, Chan and Choy performed mass, territory-wide single time point AF screening in Hong Kong, whereby amongst 13,122 participants, AF prevalence was 1.8 % and newly diagnosed AF was 0.8 %<sup>43</sup>. Although there are several limitations in the screening method, nearly half of the patients were newly diagnosed by the smartphone-based personal ECG device. Thus, population screening methods have the potential to increase AF diagnosis rates at varying costs, and the feasibility and cost-effectiveness of a smartphone-based screening tool remains unknown.

Because non-paroxysmal AF patients without clinical symptoms are especially common in elderly population, systematic screening of older population may improve the prevalence of AF<sup>33</sup>. However, systematic screening through single ECG recording may underestimate

paroxysmal AF. Thus, to detect paroxysmal AF, prolonged ECG monitoring or repeated ECG recording is required. As another example of systematic AF screening, 7,173 participants of the STROKESTOP study were screened by intermittent ECG recordings over 2 weeks<sup>44</sup>. Of this cohort, 9.3 % had a previous AF diagnosis and AF was found in 0.5 % on their first ECG. The final prevalence of AF confirmed by repeated ECG recordings (average 26.4 ECG recordings per subject) over 2 weeks was increased to 12.3 %, compared to 9.3 % that was reported before the screening exercise.

Large-scale AF screening studies including more than 5,000 participants are listed and summarized in table 1. In terms of the additive diagnostic yield and the number needed to screen for one patient with newly diagnosed AF, repeated ECG recording was the most useful for screening<sup>44</sup>. Although it is difficult to make general conclusions about the additive diagnostic yield of AF screening, given the different characteristics of the populations studied, such as race, age, and screening methods chosen, AF prevalence acquired from screening was higher than that of the existing diagnostic framework. Efforts are needed to develop and validate screening methods across various populations that are both accurate and cost-effective, particularly in a publicly-funded universal health care system.

### **Future perspectives of AF screening**

Due to rapid technological advances and cost savings, systematic population screening for AF is becoming an increasingly feasible approach and this might enable us to discover and treat more AF patients, previously undetected and untreated. Because it is well known that patients with SCAF have higher stroke risk<sup>12, 13, 18, 20</sup>, it is anticipated that early anticoagulation, when carefully determined according to AF burden, may be beneficial in terms of stroke prevention,

and prospective studies are investigating this<sup>28, 29, 44</sup>. With current screening methods, diagnoses can only be made after a certain degree of AF is evident.

Through the accumulation of imaging technologies and related investigations, we have found that AF is not merely an abnormal pulse, but a syndrome associated with myocardial remodelling represented by progressive atrial fibrosis<sup>45,46</sup>. Although the evidence to support the imaging-based screening is scarce, Healey et al. demonstrated the predictive value of echocardiographic changes in left atrial size for AF in the ASSERT-II trial<sup>47</sup>. However, the extent of left atrial size change may be too small to reflect the degree of atrial remodelling in the subclinical stage of AF (HR per centimetre diameter, 1.43; 95% CI 1.11–2.15)<sup>47</sup>. Therefore, the development of more advanced, sensitive and reliable diagnostic imaging techniques may facilitate the differentiation of SCAF before the clinical phase of AF (Figure 1). In order to realize imaging-based screening, more evidence will be needed. Indeed, imaging-based screening technology may potentially have several advantages over the ECG based approach. Without CIEDs, ECGs can miss SCAF events if they cannot be recorded at the time of event, but the possibility of missing an unpredictable SCAF event disappears through evaluation of ‘static’ atrial substrate by imaging tools regardless of ‘dynamic’ rhythm status. Furthermore, a single examination can assess all objective aspects of substrate, instead of repeated recordings over a long period (usually, several dozens or hundreds of recordings are required, but are not satisfactory)<sup>21,44</sup>. Because imaging for screening will be performed when the patient is in sinus rhythm state, commonly issued limitations of atrial imaging technology in AF patients are mostly reduced or eliminated, and even more delicate imaging acquisition and analysis will be realized in the future AF screening.

Screening of AF is of great importance in the prevention of ischemic stroke, which is a

socially and medically substantial issue. AF screening becomes increasingly feasible given the technological advances and more comprehensive understanding of AF pathophysiology. Patient perspectives are important, and most patients place great emphasis on stroke prevention although adherence to treatment efforts require emphasis and implementation<sup>48, 49</sup>. Only then, all screening efforts will lead to greater AF awareness and detection, as well as an improvement in outcomes.

## **DISCLOSURES**

**GL:** Consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseen and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally

**SYS:** None declared

## References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation*. 2014;129:837-847.
2. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *Am J Cardiol*. 2013;112:1142-1147.
3. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001;285:2370-2375.
4. Bjorck S, Palaszewski B, Friberg L, Bergfeldt L. Atrial fibrillation, stroke risk, and warfarin therapy revisited: a population-based study. *Stroke*. 2013;44:3103-3108.
5. Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: a systematic review. *Am J Med*. 2006;119:448 e441-419.
6. Wachter R, Freedman B. The role of atrial fibrillation in patients with an embolic stroke of unknown source (ESUS). *Thromb Haemost*. 2017;117:1833-1835.
7. Bruggenjurgan B, Rossnagel K, Roll S, et al. The impact of atrial fibrillation on the cost of stroke: the berlin acute stroke study. *Value Health*. 2007;10:137-143.
8. Lip G, Freedman B, De Caterina R, Potpara TS. Stroke prevention in atrial fibrillation: Past, present and future. Comparing the guidelines and practical decision-making. *Thromb Haemost*. 2017;117:1230-1239.
9. Daoud EG, Glotzer TV, Wyse DG, et al. Temporal relationship of atrial tachyarrhythmias, cerebrovascular events, and systemic emboli based on stored

- device data: a subgroup analysis of TRENDS. *Heart Rhythm*. 2011;8:1416-1423.
10. Brambatti M, Connolly SJ, Gold MR, et al. Temporal relationship between subclinical atrial fibrillation and embolic events. *Circulation*. 2014;129:2094-2099.
  11. Martin DT, Bersohn MM, Waldo AL, et al. Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices. *Eur Heart J*. 2015;36:1660-1668.
  12. Boriani G, Glotzer TV, Santini M, et al. Device-detected atrial fibrillation and risk for stroke: an analysis of >10,000 patients from the SOS AF project (Stroke preventiOn Strategies based on Atrial Fibrillation information from implanted devices). *Eur Heart J*. 2014;35:508-516.
  13. Camm AJ, Simantirakis E, Goette A, et al. Atrial high-rate episodes and stroke prevention. *Europace*. 2017;19:169-179.
  14. Gorenek BC, Bax J, Boriani G, et al. Device-detected subclinical atrial tachyarrhythmias: definition, implications and management-an European Heart Rhythm Association (EHRA) consensus document, endorsed by Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). *Europace*. 2017;19:1556-1578.
  15. Adams HP, Jr., Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke*. 1993;24:35-41.
  16. Hart RG, Diener HC, Coutts SB, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol*. 2014;13:429-438.
  17. Hart RG, Catanese L, Perera KS, Ntaios G, Connolly SJ. Embolic Stroke of

- Undetermined Source: A Systematic Review and Clinical Update. *Stroke*. 2017;48:867-872.
18. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med*. 2012;366:120-129.
  19. Healey JS, Martin JL, Duncan A, et al. Pacemaker-detected atrial fibrillation in patients with pacemakers: prevalence, predictors, and current use of oral anticoagulation. *Can J Cardiol*. 2013;29:224-228.
  20. Glotzer TV, Hellkamp AS, Zimmerman J, et al. Atrial high rate episodes detected by pacemaker diagnostics predict death and stroke: report of the Atrial Diagnostics Ancillary Study of the MOde Selection Trial (MOST). *Circulation*. 2003;107:1614-1619.
  21. Ziegler PD, Glotzer TV, Daoud EG, et al. Detection of previously undiagnosed atrial fibrillation in patients with stroke risk factors and usefulness of continuous monitoring in primary stroke prevention. *Am J Cardiol*. 2012;110:1309-1314.
  22. Ziegler PD, Glotzer TV, Daoud EG, et al. Incidence of newly detected atrial arrhythmias via implantable devices in patients with a history of thromboembolic events. *Stroke*. 2010;41:256-260.
  23. Shanmugam N, Boerdlein A, Proff J, et al. Detection of atrial high-rate events by continuous home monitoring: clinical significance in the heart failure-cardiac resynchronization therapy population. *Europace*. 2012;14:230-237.
  24. Glotzer TV, Daoud EG, Wyse DG, et al. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: the TRENDS study. *Circ Arrhythm Electrophysiol*. 2009;2:474-480.
  25. Botto GL, Padeletti L, Santini M, et al. Presence and duration of atrial fibrillation

- detected by continuous monitoring: crucial implications for the risk of thromboembolic events. *J Cardiovasc Electrophysiol.* 2009;20:241-248.
26. Capucci A, Santini M, Padeletti L, et al. Monitored atrial fibrillation duration predicts arterial embolic events in patients suffering from bradycardia and atrial fibrillation implanted with antitachycardia pacemakers. *J Am Coll Cardiol.* 2005;46:1913-1920.
  27. Van Gelder IC, Healey JS, Crijns H, et al. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J.* 2017;38:1339-1344.
  28. Lopes RD, Alings M, Connolly SJ, et al. Rationale and design of the Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial. *Am Heart J.* 2017;189:137-145.
  29. Kirchhof P, Blank BF, Calvert M, et al. Probing oral anticoagulation in patients with atrial high rate episodes: Rationale and design of the Non-vitamin K antagonist Oral anticoagulants in patients with Atrial High rate episodes (NOAH-AFNET 6) trial. *Am Heart J.* 2017;190:12-18.
  30. Wiesel J, Salomone TJ. Screening for Atrial Fibrillation in Patients  $\geq 65$  Years Using an Automatic Blood Pressure Monitor in a Skilled Nursing Facility. *Am J Cardiol.* 2017;120:1322-1324.
  31. Verberk WJ, Omboni S, Kollias A, Stergiou GS. Screening for atrial fibrillation with automated blood pressure measurement: Research evidence and practice recommendations. *Int J Cardiol.* 2016;203:465-473.
  32. Davis RC, Hobbs FD, Kenkre JE, et al. Prevalence of atrial fibrillation in the general population and in high-risk groups: the ECHOES study. *Europace.* 2012;14:1553-1559.

33. Lowres N, Neubeck L, Redfern J, Freedman SB. Screening to identify unknown atrial fibrillation. A systematic review. *Thromb Haemost.* 2013;110:213-222.
34. Mant J, Fitzmaurice DA, Hobbs FD, et al. Accuracy of diagnosing atrial fibrillation on electrocardiogram by primary care practitioners and interpretative diagnostic software: analysis of data from screening for atrial fibrillation in the elderly (SAFE) trial. *BMJ.* 2007;335:380.
35. Taggar JS, Coleman T, Lewis S, Heneghan C, Jones M. Accuracy of methods for detecting an irregular pulse and suspected atrial fibrillation: A systematic review and meta-analysis. *Eur J Prev Cardiol.* 2016;23:1330-1338.
36. Rizos T, Guntner J, Jenetzky E, et al. Continuous stroke unit electrocardiographic monitoring versus 24-hour Holter electrocardiography for detection of paroxysmal atrial fibrillation after stroke. *Stroke.* 2012;43:2689-2694.
37. Grond M, Jauss M, Hamann G, et al. Improved detection of silent atrial fibrillation using 72-hour Holter ECG in patients with ischemic stroke: a prospective multicenter cohort study. *Stroke.* 2013;44:3357-3364.
38. Zink MD, Marx N, Crijns HJGM, Schotten U. Opportunities and challenges of large-scale screening for atrial fibrillation. *Herzschrittmachertherapie und Elektrophysiologie.* 2018;29:57-61.
39. Allan V, Honarbakhsh S, Casas JP, et al. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. *Thromb Haemost.* 2017;117:837-850.
40. Welton NJ, McAleenan A, Thom HH, et al. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis. *Health Technol Assess.*

- 2017;21:1-236.
41. Lowres N, Neubeck L, Salkeld G, et al. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. *Thromb Haemost.* 2014;111:1167-1176.
  42. Halcox JPJ, Wareham K, Cardew A, et al. Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation: The REHEARSE-AF Study. *Circulation.* 2017;136:1784-1794.
  43. Chan NY, Choy CC. Screening for atrial fibrillation in 13 122 Hong Kong citizens with smartphone electrocardiogram. *Heart.* 2017;103:24-31.
  44. Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study. *Circulation.* 2015;131:2176-2184.
  45. Gal P, Marrouche NF. Magnetic resonance imaging of atrial fibrosis: redefining atrial fibrillation to a syndrome. *Eur Heart J.* 2017;38:14-19.
  46. Donal E, Lip GY, Galderisi M, et al. EACVI/EHRA Expert Consensus Document on the role of multi-modality imaging for the evaluation of patients with atrial fibrillation. *Eur Heart J Cardiovasc Imaging.* 2016;17:355-383.
  47. Healey JS, Alings M, Ha A, et al. Subclinical Atrial Fibrillation in Older Patients. *Circulation.* 2017;136:1276-1283.
  48. Loewen PS, Ji AT, Kapanen A, McClean A. Patient values and preferences for antithrombotic therapy in atrial fibrillation. A Narrative Systematic Review. *Thromb Haemost.* 2017;117:1007-1022.
  49. Raparelli V, Proietti M, Cangemi R, Lip GY, Lane DA, Basili S. Adherence to oral anticoagulant therapy in patients with atrial fibrillation. Focus on non-vitamin K

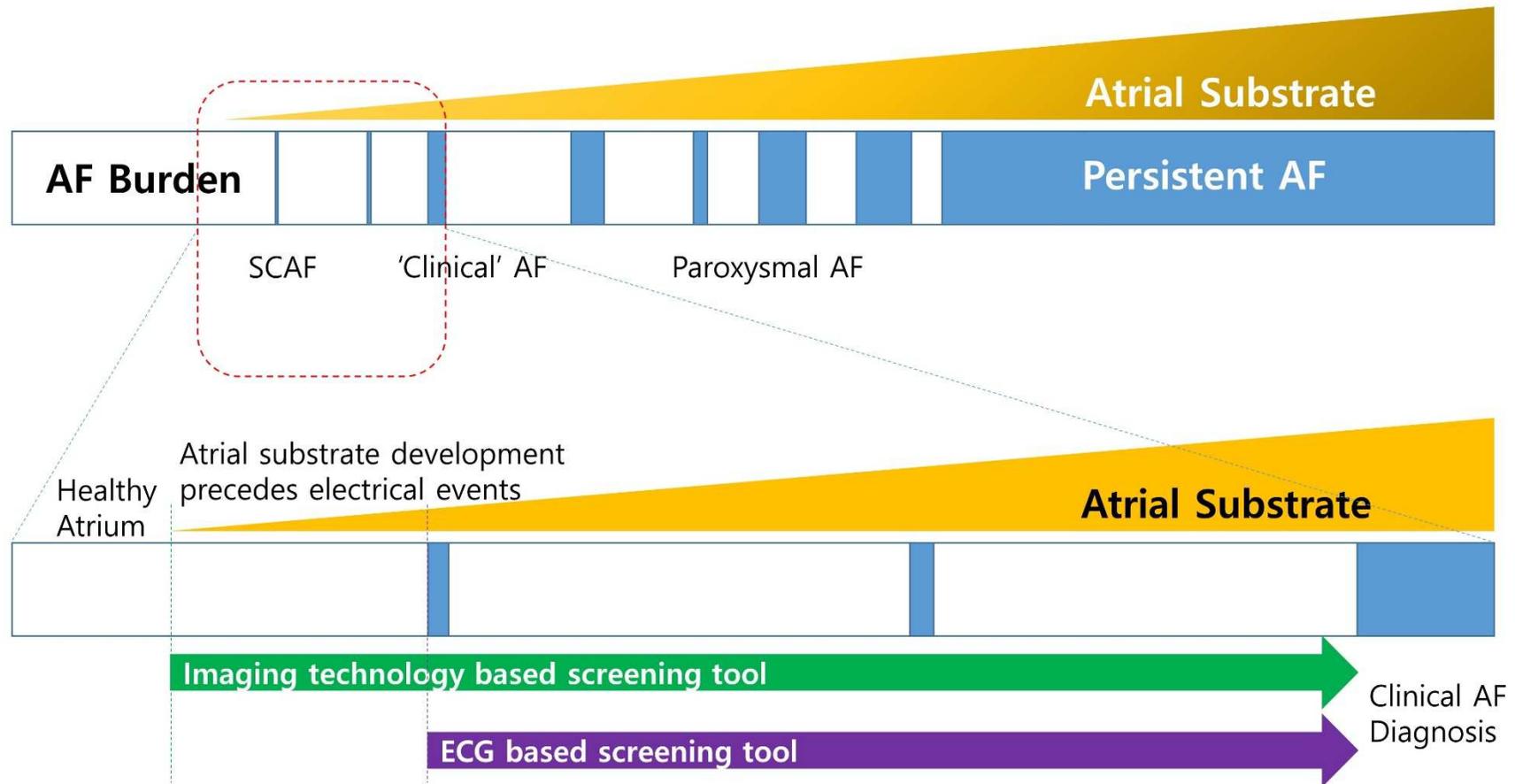
- antagonist oral anticoagulants. *Thromb Haemost.* 2017;117:209-218.
50. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in elderly subjects (the Cardiovascular Health Study). *Am J Cardiol.* 1994;74:236-241.
51. Meschia JF, Merrill P, Soliman EZ, et al. Racial disparities in awareness and treatment of atrial fibrillation: the REasons for Geographic and Racial Differences in Stroke (REGARDS) study. *Stroke.* 2010;41:581-587.
52. Proietti M, Mairesse GH, Goethals P, et al. A population screening programme for atrial fibrillation: a report from the Belgian Heart Rhythm Week screening programme. *Europace.* 2016;18:1779-1786.

Table 1. Large-scale atrial fibrillation screening studies (total number of participants &gt; 5,000)

Study	Number of participants	Target population	Mean age (yrs.)	Screening tool	Total AF prevalence N (%)	Newly diagnosed AF N (%)	NNS
Furberg et al. 1994 <sup>50</sup>	5,151	Random sample of citizens from Medicare eligibility lists from four US communities	57.6	12-lead ECG	227 (5.4)	77 (1.5)	67
Meschia et al. 2010 <sup>51</sup>	29,861	Black Americans and residents of the southeastern 'stroke belt region' in the US	74.0	7- or 12-lead ECG	432 (1.4)	174 (0.6)	172
Svennberg et al. 2015 <sup>44</sup>	7,173	75-76 year-old population in Stockholm county or the Halland region in Sweden	N/A	1-lead ECG, 2/day, 2 weeks	884 (12.3)	218 (3.0)	33
Chan et al. 2017 <sup>43</sup>	13,122	Untargeted voluntary participation by Hong Kong citizens aged $\geq 18$ years	64.7	1-lead ECG	239 (1.8)	101 (0.8)	129
Proietti et al. 2016 <sup>52</sup>	65,747	Untargeted voluntary participation by Belgian citizens	58.0	1-lead ECG	911 (1.4)	603 (0.9)	109

AF: atrial fibrillation; NNS: number needed to screen for one patient with newly diagnosed atrial fibrillation; N/A: not applicable.

Figure 1. Future of AF screening



AF: atrial fibrillation; SCAF: subclinical atrial fibrillation; ECG: electrocardiography.

