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Early detection of occult atrial fibrillation and stroke prevention

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ABSTRACT

Atrial fibrillation (AF) is a very common arrhythmia and significantly increases stroke risk. This risk can be mitigated with oral anticoagulation, but AF is often asymptomatic, or occult, preventing timely detection and treatment. Accordingly, occult AF may cause stroke before it is clinically diagnosed. Currently, guidelines for the early detection and treatment of occult AF are limited. This review addresses recent advancements in occult AF detection methods, identification of populations at high risk for occult AF, the treatment of occult AF with oral anticoagulation, as well as ongoing trials that may answer critically important questions regarding occult AF screening.

INTRODUCTION

Atrial Fibrillation (AF) is a common arrhythmia, affecting more than 2.7 million Americans and 6 million Europeans.[1 2] However, at least a third of patients with AF are asymptomatic. Furthermore, only a fifth of symptomatic AF patients will have symptoms temporally related to their AF episodes.[3–5] Accordingly, the prevalence of AF may be much higher than has been previously reported. Undiagnosed, or occult, AF may exist undetected indefinitely, be diagnosed incidentally, or eventually result in symptoms. However, the most concerning initial presentation of occult AF is stroke (figure 1).

Occult AF is detected in a fifth of patients with acute stroke.[6 7] AF increases the risk of stroke fivefold independent of other factors.[8] Treatment with oral anticoagulation (OAC), however, can reduce the relative risk of stroke in patients with AF by two-thirds.[2] Whether similar benefit can be obtained by early anticoagulation of occult AF is uncertain.

In light of these uncertainties, this review will address four clinically relevant questions. First, is it appropriate to screen for occult AF? Second, what methods are currently available to screen for occult AF? Third, what populations might harbour high rates of occult AF? Fourth and finally, should occult AF be treated with OAC?

IS IT APPROPRIATE TO SCREEN FOR OCCULT AF?

In 1968, Drs James Wilson and Gunnar Jungner developed criteria for appropriate screening for medical conditions (box 1). Screening for occult AF meets many of the Wilson-Jungner criteria. Specifically, AF is an important health problem, has a detectable asymptomatic period, effective screening techniques exist and there are socially acceptable treatments to mitigate its risk.[9] However, the risk-benefit ratio of treating occult AF with OAC is not fully understood.

WHAT METHODS ARE AVAILABLE TO SCREEN FOR OCCULT AF?

Standard ECG screening

The gold standard for diagnosing AF is the 12-lead ECG. Current guidelines recommend opportunistic pulse palpation in patients 65 years and older followed by ECG screening if the pulse is abnormal.[10] These recommendations stem from a trial published in 2007 comparing systematic and opportunistic (ie, ECG performed only if an irregular pulse was detected) ECG screening to routine practice in patients ≥65 years in a primary care setting. Over 14 000 patients were randomly assigned to routine practice or screening ECG. The study showed that both forms of screening were equivalent to one another and superior to routine practice in AF detection (detection of AF per year, 1.63% for screening compared with 1.04% for routine practice, p=0.01).[11]

Non-invasive devices

The Holter monitor is the gold standard of ambulatory ECG monitoring. It can record 24–48 h of continuous ECG data. However, many patients cannot tolerate the electrode patches for up to 48 h, and this relatively short monitoring interval may be insufficient to detect infrequent arrhythmias. External event monitors allow for longer AF monitoring intervals. Event monitors are small, leadless, external patches that provide continuous or intermittent recording. For example, the iRhythm Technologies Zio Patch can continuously record for up to 14 days. The Zio Patch has demonstrated superiority to Holter monitoring for detection of any arrhythmia and effectively detects AF.[12 13] Other non-invasive methods for AF screening include handheld, single-lead ECG devices (Omron Heartscan), blood pressure monitors (Microlife BP A200 Plus, Omron M6) and smartphone devices (AliveCor Heart Monitor for the Apple iPhone).[14–16]

Implantable cardiac monitoring devices

The implantable loop recorder (ILR), inserted surgically using local anaesthetic, is increasingly used in the diagnoses of paroxysmal AF. The two most commonly used ILRs are Reveal from Medtronic and Confirm from St Jude Medical. Newer generations of these devices detect AF by analysing the irregularity of successive R-R intervals, though both require a minimum duration of AF. Both are currently being used in ongoing studies investigating the detection rates of occult AF in high-risk patients.[17–19]

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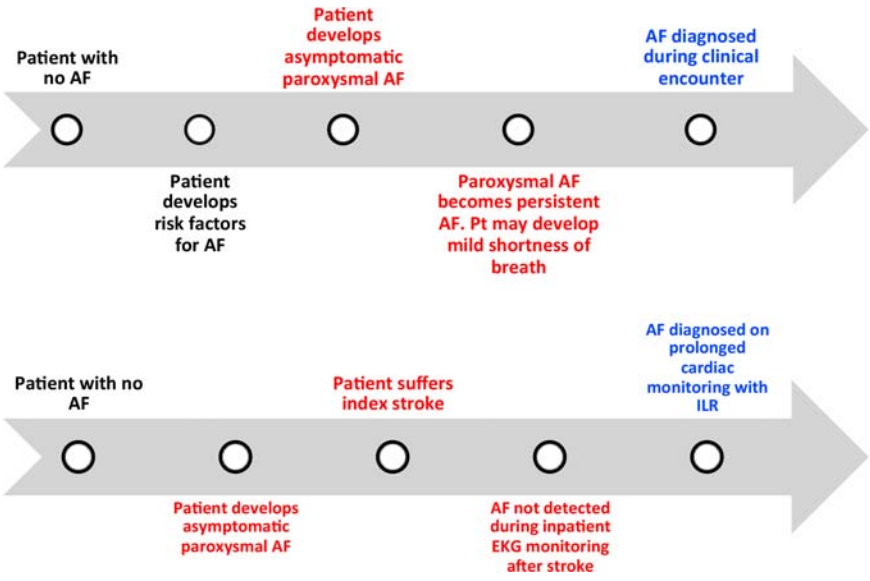

Figure 1 Occult atrial fibrillation (AF) timeline. Black text indicates no AF, red text indicates Occult AF, blue text indicates diagnosed AF. (ILR, implantable loop recorder. EKG, electrocardiogram.)

Intracardiac device interrogation

Intracardiac devices (pacemakers, implantable cardiac defibrillators, and cardiac resynchronisation therapy devices (CRTs)) have become increasingly common in the past several decades. Newer devices have the ability to store and analyse a large amount of data regarding atrial and ventricular electrical activity, with a sensitivity for AF detection nearing 98% for dual-chamber pacers.[20] However, during routine device interrogation, much of the data regarding atrial activity is of uncertain significance. As will be discussed further, the significance of device-detected atrial high rate episodes (AHREs) (ie, AF/atrial tachycardia (AT)) is difficult to interpret when the episodes are infrequent and brief.

WHAT POPULATIONS MIGHT HARBOUR HIGH RATES OF OCCULT AF?

Identifying patient populations at high risk for occult AF may provide a more targeted and higher yield AF screening approach. The following subgroups may represent high-yield populations for screening.

Box 1 Wilson-Jungner classic screening criteria

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

Cryptogenic stroke population

A quarter of strokes has no clear cause and is deemed 'cryptogenic' in nature.[21] Occult AF may be the underlying cause of many of these strokes, and two recently published trials, Cryptogenic Stroke and Underlying AF (CRYSTAL-AF) and Event Monitor Belt for Recording Atrial Fibrillation after a Cerebral Ischaemic Event (EMBRACE), investigated this possibility.[22 23] The CRYSTAL-AF trial used an implantable cardiac monitor to detect episodes of AF >30 s. The device detected AF in 8.9% of patients at 6 months and 12.4% at 12 months, as compared with rates of 1.4% at 6 months and 2.0% at 12 months in control patients (6-month absolute difference 7.5%, 95% CI 1.9% to 21.7%).[23] The EMBRACE trial used a non-invasive dry-electrode belt to detect AF episodes >30 s. After 30 days of monitoring, AF had been detected in 16.1% of monitored patients, compared with 3.2% of control patients (absolute difference 12.9%, 95% CI 8.0% to 17.6%).[22]

In this population where no other explanation for stroke could be found, occult AF seems a likely culprit. However, several important caveats to these studies warrant consideration and further investigation. First, the primary end point in both trials, detection of an episode of AF greater than 30 s, was arbitrarily defined. There is no evidence to suggest that 30 s of AF postcryptogenic stroke is more clinically relevant than shorter periods of AF. Furthermore, treatment strategies in this population are unclear. A single 30 s episode of AF may not confer the same stroke risk as a more prolonged episode of AF, and thus not warrant OAC and its attendant bleeding risk. Second, ischaemic injury to certain parts of the brain can cause transient atrial arrhythmias, so-called neurogenic AF.[24] As a result, AF may occur after an ischaemic stroke and not be the culprit for the event, thus complicating treatment decisions for occult AF identified in this setting. Finally, the time-to-initiation of cardiac monitoring was highly variable between trials. CRYSTAL-AF allowed initiation of monitoring 90 days from the index stroke, while EMBRACE allowed a window of 6 months from index stroke to monitoring. Thus, there is no clear consensus on when prolonged cardiac monitoring should be initiated after a cryptogenic stroke.

Intracardiac device population

Atrial high rate episodes (AHREs) are exceedingly common during device interrogation and can be detected in approximately half of patients with intracardiac devices.[25 26] The

definition of an AHRE varies between trials, but is generally defined as an episode of AF/AT with an atrial rate greater than 175–190 beats per minute (bpm).

The first trial to demonstrate a link between AHREs and worsened outcomes was a subgroup analysis of Mode Selection Trial, published in 2003. It revealed that patients with at least one 5-min or longer AHRE >220 bpm had a 2.8-fold increased risk of stroke or death and a 5.9-fold increased risk of developing permanent AF.[25] The 2009 TRENDS trial showed that patients with a daily burden of AHRE >5.5 h had a 2.4-fold increase in the risk of thromboembolism.[26] A 2012 study by Shanmugam *et al*[27] demonstrated that in patients with heart failure and a CRT device, an AHRE >180 bpm for more than 3.8 h/day was associated with a ninefold increase in thromboembolic events.

Furthermore, the 2012 Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT) found that in patients *without* a prior diagnosis of AF, an AHRE of at least 6 min and >190 bpm was associated with a 2.5-fold increase in the risk of stroke or systemic embolism.[28] Finally, in a pooled analysis of more than 10 000 relatively unselected patients, the 2014 Stroke Prevention Strategies Based on AF Information from Implanted Devices project (SOS AF), found that an AHRE lasting longer than 1 h was associated with a 2.1-fold increased risk of ischaemic stroke.[29]

The above trials demonstrate a clear association between device-detected AHREs and poor clinical outcomes. However, as in the cryptogenic stroke population, this association does not prove causation. For example, only weak temporal associations between AHREs and subsequent stroke were seen in subanalyses of the TRENDS and ASSERT trials; only 30% and 15% of patients, respectively, had an AHRE within the month leading up to their stroke.[26 30] Thus, AHREs may simply be a risk marker for a diseased cardiovascular system more prone to stroke, rather than a direct cause of stroke.

Furthermore, the above trials used varying definitions of significant AHRE duration. The TRENDS trial required a daily burden of AHREs greater than 5.5 h to demonstrate worsened clinical outcomes, while the ASSERT study required only a single episode greater than 6 min. Finally, there is no clear evidence that treatment with OAC will reduce the risk of stroke in this population.

Elderly population

AF is common in the elderly, with rates as high as 23.5% in those aged 80 years or older.[1] As mentioned above, a 2007 trial detected AF in 1.6% of patients greater than 65 years old with a single screening ECG.[11] Similarly, a 2013 study screened patients aged 75 years and 76 years with twice-daily ECGs for 2 weeks. Patients had a Patients had a CHADS2 score (Congestive Heart Failure (CHF), Hypertension (HTN), Age ≥75, Diabetes, Stroke (2 points)) ≥2 and no prior history of AF. With this relatively simple screening method, 30/403 (7.4%) patients were diagnosed with previously unknown AF.[31] Thus, screening programmes in this population are likely to be high-yield.

Risk model estimated high-risk population

While the above specific age cut-offs or disease states may represent convenient groups for screening, this approach may miss large populations at risk for occult AF. Accordingly, models have been developed to assist in AF risk stratification. The Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) model, published in 2013, was developed using data from three large American cohorts and subsequently validated in two large European cohorts.[32] The analysis identified 11 readily available factors for use in a 5-year risk model: age, race, height, weight, systolic and diastolic blood pressures, current smoking status, use of antihypertensive medication, diabetes, history of myocardial infarction and history of heart failure (CHARGE simple model). The predictive model achieved good discrimination in the derivation cohorts (C-statistic, 0.765; 95% CI 0.748 to 0.781) and modest to good discrimination in the validation cohorts (C-statistics, 0.664 and 0.705).

Another model, published in 2014 by Brunner *et al*,[33] investigated the performance of seven previously identified risk factors for AF in a cohort of nearly 100 000 patients. The risk factors included: age, coronary artery disease, diabetes mellitus, sex, heart failure, hypertension and valvular disease. From this information a simple seven-factor risk calculator was derived which produces a score of 0–12. The area under the curve statistic for the AF risk score was 0.812 (95% CI 0.805 to 0.820). The ORs of subsequent AF diagnosis of patients with AF risk scores of 1, 2, 3, 4 and 5, or higher were 3.05, 12.9, 22.8, 34.0 and 48.0, respectively. It is important to note that both of the above models do not require ECG or laboratory data, thus increasing the potential for widespread use.

A recent study investigated the effectiveness of risk factor based screening. The Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF) investigated the incidence of occult AF in high-risk patients (age ≥55 years and at least two risk factors: coronary artery disease, heart failure, hypertension, diabetes, sleep apnoea) but with no history of AF. Participants wore an event monitor for 2 weeks. Sustained AF/AT ≥60 s was noted in more than 10% of patients.[34]

Additionally, two ongoing trials are investigating the effectiveness of screening using the widely known CHADS2 and CHA2DS2-VASc scores (CHF, HTN, Age ≥75 (2 points), Diabetes, Stroke (2 points), Vascular Disease, Age ≥65 years (1 point), Female Sex). REVEAL-AF is a prospective study evaluating the incidence of AF ≥6 min in patients at high risk for AF (CHADS2 ≥2) but with no history of AF. Patients will have a subcutaneous monitor implanted (Medtronic) and monitored for AF and thromboembolic events.[19] ASSERT-II is a prospective study investigating detection of AF ≥5 min with an implanted subcutaneous monitor (St Jude's) in patients with no prior diagnoses of AF but who are at high risk for developing AF (CHA2DS2-VASc ≥2)[35] (table 1).

Other measures to identify risk of occult AF

A variety of biomarkers, ECG findings and echocardiogram parameters have been associated with AF. Elevation of B-type natriuretic peptide or cardiac troponin after stroke or transient ischaemic attack is associated with new AF.[36 37] P-wave duration on standard ECG can predict new-onset AF.[38] Atrial ectopy after standard exercise testing can predict AF in subjects with left ventricular hypertrophy.[39] Finally, echocardiographic evidence of left atrial size and left atrial dysfunction are strong predictors of incident AF, as well as stroke independent of clinical AF.[40 41]

SHOULD OCCULT AF BE TREATED WITH OAC?

Given viable methods available for AF screening, and easily identifiable populations at high enough AF risk to warrant screening, the questions remains: will occult AF show the same benefit from treatment with OAC as traditionally detected AF?

Traditionally detected AF is routinely classified as one of three types: paroxysmal, persistent or permanent (paroxysmal

Table 1 Summary of ongoing trials investigating the diagnoses of occult AF

	Population	Intervention	Primary outcomes	Impact on current understanding
REVEAL-AF	CHADS2 ≥3, or ≥2 +CAD, CKD, OSA or COPD *No history of AF*	Insertion of ILR	AF episode >6 min, thromboembolism	Will further understanding of risk factors for occult AF, ILR for detection of AF >6 min, temporal relationship between AF episode and stroke
ASSERT-II	Age ≥65 +CHA2DS2-VASc ≥2 +LA enlargement or elevated p-BNP *No history of AF*	Insertion of ILR	AF episode >5 min, thromboembolism	Will further understanding of risk factors for occult AF, ILR for detection of AF >5 min, temporal relationship between AF episode and stroke

AF, atrial fibrillation; ASSERT, Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CHADS2, CHF, HTN, Age ≥75, Diabetes, Stroke (2 points); CHA2DS2-VASc, CHF, HTN, Age ≥75 (2 points), Diabetes, Stroke (2 points), Vascular Disease, Age ≥65 (1 point), Female Sex; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; LA, left atrial; ILR, implantable loop recorder; OSA, obstructive sleep apnoea.

AF being short and intermittent bursts of AF, while persistent and permanent AF are more prolonged or constant).[42] Current guidelines recommend treating AF based on clinical risk factors, not by the type or duration of AF.[2] However, data on the correlation between AF duration and stroke is conflicting. Several studies suggest that paroxysmal, persistent and permanent AF carry the same risk of stroke while others suggest that stroke risk correlates with AF duration.[43 44] This conflicting data complicates the management of occult AF.

If occult, *permanent* AF is detected on routine pacer interrogation or after an index stroke, treatment with OAC should be considered based on clinical risk factors. However, current evidence does not offer specific treatment recommendations for occult, *paroxysmal* AF. The duration and frequency of occult, paroxysmal AF that lead to increased risk of stroke are poorly defined. Thus, the burden of occult, paroxysmal AF necessary to warrant OAC treatment is unclear. Several studies are underway that may shed light on these questions.

Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) is a prospective, randomised, double-blinded trial investigating the benefit of anticoagulation in the device-detected AHRE population. It will compare treatment with aspirin 81 mg to apixaban 5 mg twice daily in patients with device-detected AHREs but no history of clinical AF. Primary outcomes will be stroke and major bleeding events. Results are expected in 2019.[45]

Systematic ECG Screening for Atrial Fibrillation Among 75-year-old Subjects in the Region of Stockholm and Halland, Sweden (STROKESTOP) is a randomised, parallel-assignment trial investigating the effectiveness of population-wide AF screening combined with subsequent OAC treatment. This study will directly test the hypothesis that screening for occult AF can reduce the rates of stroke. All persons aged 75 years and 76 years with no history of AF will be randomised to either 2 weeks of twice-daily ECG screening or routine care. Those with AF duration >30 s will be offered treatment with OAC. Primary outcomes will be stroke and major bleeding events and results are expected in 2019.[46] Results from ARTESiA and STROKESTOP will be critically important in demonstrating the benefit derived from screening for, and subsequently treating, occult AF (table 2).

Two other trials will evaluate the *initiation* or *withdrawal* of OAC via remote monitoring in patients with a *prior history of AF* but with low burden of device-detected AF. Rhythm Evaluation for Anticoagulation With Continuous Monitoring (REACT COM) is a prospective, non-randomised study evaluating the safety and efficacy of intermittent anticoagulation with a rapid-onset novel OAC guided by a continuous AF-sensing implantable cardiac monitor (Medtronic Reveal XT) with remote data transmission capabilities.[47] Tailored Anticoagulation for Non-continuous AF (TACTIC-AF) is a prospective, randomised study involving patients already taking a novel OAC for paroxysmal AF, investigating if discontinuing OAC in patients with little to no detectable AF can improve outcomes of stroke and major bleeding events[48] (table 3).

Both studies are similar in design to the prematurely terminated Randomised Trial of Anticoagulation Guided by Remote Rhythm Monitoring in Patients With Implanted Cardioverter-Defibrillator and Resynchronisation Devices (IMPACT). IMPACT tested the hypothesis that initiation and/or withdrawal of oral anticoagulant therapy based on the presence or absence of AHREs by remote monitoring via CRT-D devices could reduce major-bleeding events while still preventing thromboembolic events.[49] IMPACT was stopped prematurely based on failure to demonstrate a meaningful difference between arms. Despite the intervention arm's earlier initiation of OAC (remote monitoring vs control, 3 days vs 54 days; $p<0.001$), no significant difference was noted in the primary outcome.[50] This lack of difference likely reflects the complex relationship between AF, comorbid risk factors and stroke. Those at highest risk for AF related stroke are also at high risk for non-AF related strokes, and as such, targeting OAC therapy only to times of high AF burden may not be the most effective strategy for stroke prevention.

Table 2 Summary of ongoing trials investigating the safety/efficacy of OAC treatment of occult AF

	Population	Intervention	Primary outcomes	Impact on current understanding
ARTESiA	CHA2DS2-VASc ≥4 with at least a single AHRE ≥175 bpm lasting ≥6 min detected by ILR or intracardiac device *No history or ECG evidence of clinical AF*	Randomised to either aspirin 81 mg daily (control) or apixaban 5 mg twice daily (intervention)	Incidence of stroke and major bleeding events	Will be the first trial directly investigating the risk/benefit of OAC treatment in the device-detected AHRE population.
STROKESTOP	All persons aged 75 years and 76 years in two Swedish provinces *No history of AF*	Twice-daily ECG screening+OAC treatment if AF detected (single episode duration >30 s, or 2 or more episodes >10 s)	Incidence of stroke and major bleeding events	Will be the first trial investigating population-based screening for occult AF and the effect on stroke prevention

AF, atrial fibrillation; AHREs, atrial high rate episodes; ARTESiA, Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation; CHA2DS2-VASc, CHF, HTN, Age ≥75 (2 points), Diabetes, Stroke (2 points), Vascular Disease, Age ≥65 (1 point), Female Sex; ILR, implantable loop recorder; OAC, oral anticoagulation.

Table 3 Summary of ongoing trials investigating the cessation and/or reinitiation of OAC based on AF burden

	Population	Intervention	Primary outcomes	Impact on current understanding
REACT COM	CHADS2 of 1 or 2, recently implanted Medtronic REVEAL XT loop recorder No permanent AF or recent AF episode lasting >1 h	Rapid initiation of 30 days of NOAC therapy following a remotely detected episode of AF	OAC utilisation, incidence of stroke, death and major bleeding events	Will demonstrate safety/efficacy of treating paroxysmal or persistent AF with NOAC only during times temporally related to AF episodes (other studies have demonstrated a weak temporal relationship between episodes of AF and stroke)
TACTIC-AF	History of paroxysmal or persistent AF currently taking NOAC+intracardiac device (St Jude) No permanent AF	Withdrawal/reinitiation of NOAC based on remote-monitoring of atrial activity (AT/AF)	Incidence of stroke, death, cardiovascular complications	Will demonstrate the safety of OAC cessation in patients with low AF burden, temporal relationship between stroke and AF, effect of weekly remote device interrogation

AF, atrial fibrillation; AT, atrial tachycardia; CHA2DS2-VASc, CHF, HTN, Age ≥75 (2 points), Diabetes, Stroke (2 points), Vascular Disease, Age ≥65 (1 point), Female Sex; NOAC, novel oral anticoagulation (ie, dabigatran); OAC, oral anticoagulation; REACT COM, Rhythm Evaluation for Anticoagulation With Continuous Monitoring; TACTIC-AF, Tailored Anticoagulation for Non-continuous AF.

CONCLUSIONS

Screening for occult AF fulfils many criteria for appropriate medical screening. Most importantly, occult AF has a detectable asymptomatic period and a treatment to reliably mitigate the risk of stroke. However, several unanswered questions remain regarding occult AF screening. First, what burden of occult AF is necessary to increase the risk of stroke and thus show benefit from OAC treatment? Second, will mass screening and treatment of occult AF effectively reduce the risk of associated stroke? While these questions currently remain unanswered, numerous trials are underway that will hopefully advance our understanding of occult AF significantly (table 4).

Table 4 Conclusions

Should we screen for occult AF?	Screening for AF fulfils many of the Wilson-Jungner criteria. However, the overall benefit and cost-effectiveness of screening has yet to be demonstrated. Ongoing trials that may answer this question include: *STROKESTOP*
How should we screen for occult AF?	There are many viable options for screening. Non-invasive methods such as opportunistic ECGs, event monitors, single-lead ECGs, blood pressure monitors and smartphone applications can reliably detect occult AF. Invasive methods such as intracardiac device interrogation or implantable loop recorders (ILRs) are very high-yield in appropriate populations. Trials comparing various screening methods are needed
Who should we screen for occult AF?	Those with cryptogenic strokes, intracardiac devices and advanced age are likely appropriate for routine screening. Risk-model based screening has the potential to identify a high-risk subgroup in a much larger population. Ongoing trials that may answer this question include: *REVEAL AF* and *ASSERT-II*
Does occult AF directly cause stroke?	Trials in the intracardiac device population such as TRENDS and ASSERT suggest that AHREs increase the rate of stroke. However, given the weak temporal relationship between occult AF and stroke, the mechanism by which short bursts of occult AF lead to stroke are poorly understood. Ongoing trials that may answer this question include: *REACT COM* and *TACTIC-AF*
Should occult AF be treated with OAC?	The burden of occult, paroxysmal AF needed to increase risk of stroke is not fully understood, thus the risk-benefit ratio of OAC treatment is difficult to calculate. Ongoing trials that may answer this question include: *ARTESiA*
Will screening for occult AF reduce stroke?	Ongoing trials that may answer this question include: *STROKESTOP*

AF, atrial fibrillation; AHRE, atrial high rate episode; ARTESiA, Apixaban for the Reduction of Thromboembolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation; ASSERT, Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial; REACT COM, Rhythm Evaluation for Anticoagulation With Continuous Monitoring; TACTIC-AF, Tailored Anticoagulation for Non-continuous AF.

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