UK National Screening Committee

Evidence Summary for Screening for Atrial Fibrillation in Adults

External review against programme appraisal criteria for the UK National Screening Committee

Version: FINAL

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The UK National Screening Committee secretariat is hosted by Public Health England.

About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of population screening and supports implementation of screening programmes.
Conditions are reviewed against evidence review criteria according to the UK NSC's evidence review process.

Read a complete list of UK NSC recommendations.

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Plain English summary

Atrial fibrillation (AF) is a heart condition that causes an irregular and often a faster than normal heart rate. AF can lead to an increased risk of stroke and death. The current UK NSC policy is that population screening for AF should not be offered by the National Health Service (NHS). This is based on the findings of an external review of AF against UK NSC criteria in June 2014, which evaluated studies published up to December 2011. The purpose of this rapid review was to identify any new studies published since December 2011 that would challenge or reaffirm the current recommendation on screening.

There is some recently published good quality evidence to suggest that population screening for AF is cost-effective. There is also evidence from diagnostic accuracy studies to suggest that pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings would be appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear. However, other results were less certain or there was a lack of information. In particular, no evidence was found on the effect of treating people with AF identified through screening, so the benefit of screening was not shown.

Although some criteria are met, screening is not recommended at this time.

Executive summary

Purpose of the review

The purpose of this rapid review was to identify any new publications that address the evidence gaps highlighted by the 2014 review: Screening for Atrial Fibrillation in the over 65s. London: UK National Screening Committee; June 2014. With this new evidence, we sought to establish whether there have been any significant developments that would either challenge or reaffirm the current recommendation on screening.

Background

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia that results in deterioration of the mechanical function of the atrium [1]. AF can lead to an increased risk of stroke and death [2]. The current gold standard method for diagnosing AF is by a 12-lead electrocardiogram (ECG) [3]. Other tests include alternative types of ECG and ECG in combination with pulse point monitoring [4].

Data estimates from 2015 suggest that 1.4 million people in England are living with AF, with the estimated prevalence being 2.5%. Systematic general population screening, however, is not currently recommended in the UK[5].

Focus of the review

This rapid review updates the evidence summary as part of the UK National Screening Committee (NSC) three yearly review cycle. This update, which assesses the literature published from January 2011 onwards, focuses on screening adults (≥ 65 years of age) for AF in order to inform the policy under review.

The specific questions that this rapid review sought to answer are:

1. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF, or between people with asymptomatic compared to symptomatic AF?

2. What is the benefit of treating screen-detected AF? Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?
3. What is the reported accuracy of screening tests for all types of AF?
4. Have randomised controlled trials (RCTs) demonstrated a benefit of screening for AF over and above diagnosis of AF only through clinical practice?
5. Is screening for AF in adults cost-effective?
6. Is the current clinical pathway for AF optimised in terms of patient compliance and prescribing patterns for anticoagulants?

Recommendation under review

The current UK NSC policy is that population screening for AF should not be offered by the National Health Service (NHS). This is based on the findings of an external review of AF against UK NSC criteria in June 2014 using relevant publications published until December 2011 [5]. The last evidence review summary was conducted in May 2014 [6].

Findings and gaps in the evidence of this review

Summary of Findings Relevant to Question 1, Criterion 1: Criterion uncertain

1. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF, or between people with asymptomatic compared to symptomatic AF?

Paroxysmal AF vs. persistent or permanent AF

There is consistent evidence that the number of stroke events are significantly higher in patients with permanent AF compared with paroxysmal AF, but differences in the number of stroke events between persistent AF and paroxysmal AF are less consistent. There is also consistent evidence that stroke risk (measured using mean $CHADS_2$ and CHA_2DS_2-VASc scores or the percentage of patients with $CHADS_2$ and CHA_2DS_2-VASc scores ≥2 (indicating high risk of stroke)), is significantly higher in patients with permanent AF compared with patients with paroxysmal AF. Similarly to the number of stroke events, the magnitude of difference in stroke risk between persistent AF and

paroxysmal AF is less consistent. Only one study investigated ischaemic/haemorrhagic stroke deaths, but the data were not clearly reported and no statistical comparisons were reported in this study for the groups of interest in this rapid review.

Asymptomatic vs. symptomatic AF

Results from one study demonstrated significantly more ischaemic stroke events in patients with asymptomatic AF compared to patients with symptomatic AF, but not for other types of stroke. Results for stroke risk were inconsistent between the two studies that reported these data. Two studies reported on cardiovascular death, and both reported no significant differences between patients with asymptomatic AF and symptomatic AF.

Although there are some clear patterns in the data, we cannot be certain about the study results. This is because the studies did not always use the same methods to analyse the data, and because baseline factors other than type of AF (not explored as part of this rapid review) may have had an independent impact on stroke or stroke mortality. As several data were derived from subgroup analyses, results from these analyses should be considered as exploratory only.

There are gaps in the literature regarding studies that evaluate differences in paroxysmal AF versus persistent or permanent AF on stroke mortality. There is also a general lack of literature on studies comparing asymptomatic and symptomatic AF on stroke outcomes.

Summary of Findings Relevant to Question 2, Criterion 9: Criterion not met

2. What is the benefit of treating screen-detected AF? Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?

This criterion was not met as no relevant systematic reviews or primary studies were identified that met the inclusion criteria for the review questions related to this criterion. There is clearly a lack of non-RCT comparative evidence on this topic area (see also Question 4 for RCT evidence).

Summary of Findings Relevant to Question 3, Criterion 4: Criterion met

3. What is the reported accuracy of screening tests for all types of AF?

A recent HTA of 15 diagnostic accuracy studies including over 9000 patients suggested that pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings would be appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear. Three additional recently published diagnostic studies in primary care populations that investigated pulse palpation, a portable three-lead ECG monitor and a 12-lead ECG interpreted by an algorithm support this conclusion. This criterion was met because the evidence is consistent and all studies were considered to have a low risk of bias. The harms and benefits of the interventions used in the included studies were not explored, although all were non-invasive.

Summary of Findings Relevant to Question 4, Criterion 11: Criterion not met

4. Have randomised controlled trials (RCTs) demonstrated a benefit of screening for AF over and above diagnosis of AF only through clinical practice?

Despite identifying two potentially relevant systematic reviews (which collectively, reported on only two RCTs that were subsequently deemed partly relevant to this rapid review question) and a further two recently published RCTs, it is unclear whether there is a benefit of formal screening programmes for AF over and above diagnosis of AF only through routine clinical practice. This is because the included studies did not compare formal screening to routine clinical diagnosis, or did not report relevant outcomes. An upcoming RCT has been identified, however, that may address this question in the future.

There is a lack of RCTs that compare formal screening to routine clinical diagnosis and that evaluate clinical health outcomes.

Summary of Findings Relevant to Question 5, Criterion 14: Criterion met

5. Is screening for AF in adults cost-effective?

One study in a UK setting reported on the cost-effectiveness of screening for AF. This study was considered to be at low risk of bias, and the results can be used to draw out four key findings on the cost-effectiveness of AF screening in the UK:

1. Screening for AF, whether opportunistic or population-based, is likely to be cost-effective;
2. Some form of simple initial diagnostic test before confirmation with 12-lead ECG is likely to be more cost-effective than ECG testing alone;
3. Repeat screening at five-year intervals appears to be cost-effective compared to no screening, but relative cost-effectiveness compared to single screening has not been determined;
4. The evidence of the relative cost-effectiveness of population-based screening against opportunistic screening is weak.

Summary of Findings Relevant to Question 6, Criterion 15: Criterion uncertain

6. Is the current clinical pathway for AF optimised in terms of patient compliance and prescribing patterns for anticoagulants?

Compliance/adherence to anticoagulants in the UK

One cohort study conducted in Scotland reported on medication refill adherence. In this study, 82% of patients had a medication refill adherence greater than 80%. Most studies (which reported data collected between 2011 and 2014) reported measures of continuation or persistence with anticoagulants in patients with AF who were newly prescribed anticoagulants. These percentages ranged from between 74% and 90% (across studies and types of oral anticoagulants) up to 6 months following treatment initiation, and generally appeared to decline over the treatment period, but the duration of follow-up is limited

Prescriptions foranticoagulants in the UK

Data extracted from national databases, reported directly or within studies, broadly show a general increase in prescribing rates from 2000 to 2017. These results are difficult to compare because the studies variously reported on all AF patients, patients with paroxysmal AF, or persistent/permanent AF, or patients with different risk scores.

This criterion is uncertain because although there is a sufficient volume of evidence on continuation/persistence and on prescribing, the data could not be directly compared, and because further statistical comparisons and evaluations (for example, to determine if compliance is maintained over time, or to determine if prescribing patterns are more or less optimised in patients with different types of AF or stroke risk) would need to be conducted before these questions can be fully addressed.

Recommendations on screening

- pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings are appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear
- screening for AF, whether opportunistic or population-based, is likely to be cost-effective
- although some criterion have been met, others were not met or were uncertain so that screening is not recommended at this time

Limitations

Limitations of the review methodology include a restriction on study countries. This means that some potentially relevant studies may have been missed. As this is a rapid review, the data have not been synthesised using meta-analyses, or other statistical methods. As such, some of the data should be considered as indicative only and may not comprehensively address the associated research questions.

Evidence uncertainties

There is a lack of evidence comparing formal screening programmes (including systematic and opportunistic screening programmes) over and

above diagnosis of AF through routine clinical practice on health outcomes. There were some studies that compared systematic and opportunistic screening, but they were found to be at high risk of bias. More good quality research in this area is warranted.

Measures of continuation or persistence with anticoagulants were largely collected between 2011 and 2014 and ranged from between 74% and 90% (across studies and treatment types) within 6 months of treatment initiation. Continuation or persistence levels generally appeared to decline over the treatment period. However, while reliable, these data can only be considered as descriptive and further statistical analyses would be needed to fully evaluate trends through time, or trends within a treatment period. There is a lack of well-conducted studies that measure prescription adherence and more research on this topic is needed.

There appears to have been a general increase in prescribing rates of anticoagulants in patients with AF from 2000 to 2017, however, without further statistical analyses, definitive conclusions cannot be made on any trends.

Introduction and approach

Background

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia that results in deterioration of the mechanical function of the atrium [1]. AF can occur along with other arrhythmias or on its own. There are three types of AF: paroxysmal (self-terminating), permanent or persistent (non-self-terminating). In some cases, AF can be secondary to other conditions including, but not limited to, acute myocardial infarction, pneumonia and pulmonary embolism [1]. AF can lead to an increased risk of stroke and death [2]. There is also some suggestion that this increased risk is dependent on the type of AF [4].

The symptoms of AF include palpitations, anxiety, dyspnoea, chest discomfort, sweating, fatigue and dizziness. However, in some cases the AF is 'silent' and is only diagnosed following a stroke or congestive heart failure [7].

The current gold standard method for diagnosing AF is by a 12-lead electrocardiogram (ECG) [3]. Other tests include alternative types of ECG and ECG in combination with pulse point monitoring [4].

Data estimates from 2015 suggest that 1.4 million people in England are living with AF, with the estimated prevalence being 2.5%. AF is associated with a higher prevalence in males (2.9%) than females (2.0%) [8]. The estimated global annual costs of AF per patient are 3000 Euros and the burden to society in Europe is 13.5 billion Euros [1].

Current policy context and previous reviews

A 2016 Cochrane review concluded that both systematic and opportunistic screening for AF increased the detection rate compared with routine practice. This review also suggested that there was limited evidence that the costs of opportunistic screening are lower than those for systematic screening [9]. Systematic general population screening is not currently recommended in the UK [5].

The current UK National Screening Committee (NSC) policy is that population screening for AF should not be offered by the National Health Service (NHS). This is based on the findings of an external review of AF against UK NSC criteria in June 2014 using relevant publications published until December 2011 [5]. The last evidence review summary was conducted in May 2014 [6].

The 2014 UK NSC review summary document reported that:

1. Clinical management of AF is not optimised.
2. The treatment for AF includes offering the patient long-term anticoagulants to reduce the risk of stroke if that risk is above a certain level. Many patients who would benefit from anticoagulants are not taking them. Anticoagulant treatment can last for many years.
3. Screening is likely to detect an increased number of people aged over 65 years with AF, but it would not be ethically justifiable to initiate screening in the context of concern about the management pathway.
4. There is little evidence available to determine whether the risk of progression from AF to stroke is equivalent in the screened and clinically detected populations.
5. There are concerns about operator dependency in the testing process.

Thus, there is a need to investigate whether this situation has improved.

UK National Screening Committee (UK NSC) commissioned the York Health Economics Consortium (YHEC), at the University of York, to prepare a rapid review to update the evidence summary as part of the UK NSC three yearly review cycle. This update focuses on the evidence relating to screening of adults for AF to inform the policy under review.

Objectives

The objective of this current rapid review is to identify any new publications that address the evidence gaps highlighted by the 2014 review, and to establish whether there have been any significant developments that would challenge or reaffirm the current recommendation on screening for AF.

The specific questions that this rapid review sought to answer are:

1. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF, or between people with asymptomatic compared to symptomatic AF?
2. What is the benefit of treating screen-detected AF? Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?
3. What is the reported accuracy of screening tests for all types of AF?
4. Have randomised controlled trials (RCTs) demonstrated a benefit of screening for AF over and above diagnosis of AF only through clinical practice?
5. Is screening for AF in adults cost-effective?
6. Is the current clinical pathway for AF optimised in terms of patient compliance and prescribing patterns for anticoagulants?

The screening criteria, along with the questions that address them, are presented inTable 1.

Table 1. Key questions for the evidence summary, and relationship to UK NSC screening criteria

	Criterion	Key questions	Studies Included
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence	1a. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF? 1b. Is the risk of stroke similar between people with asymptomatic	1a. Al-Khatib 2013 [10]; Banerjee 2013 [11]; Baturova 2014 [12]; Disertori 2013 [13]; Flaker 2012 [14]; Lip 2014 [15, 16]; Meinertz 2011 [17]; Proietti 2017 [18]; Steinberg 2015 [19]; Vanassche 2015 [20]. 1b. Potpara 2013 [21]; Rienstra 2014 [22].

	Criterion	Key questions	Studies Included
	about the association between the risk or disease marker and serious or treatable disease.	compared to symptomatic AF?	
9	There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered.	Question 2a – What is the benefit of treating screen-detected AF? Question 2b – Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?	2a. and 2b. No studies met the inclusion criteria for these questions.
4	There should be a simple, safe, precise and validated screening test.	Question 3 – What is the reported accuracy of screening tests for all types of AF?	Hald 2017 [23]; Kristensen 2016 [24]; Svennberg 2017 [25]; Welton 2017 [26].
11	There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity	Question 4 – Have randomised controlled trials (RCTs) demonstrated a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?	González Blanco 2017 [27]; Halcox 2017 [28]; Moran 2013 [29]; 2015 [30]; 2016 [9]; Welton 2017 [26].
14	The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criteria should have regard to evidence from cost	Question 1 – Is screening for AF in adults cost-effective?	Welton 2017 [26]

	Criterion	Key questions	Studies Included
	benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.		
15	Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme.	Question 6a – Is the current clinical pathway for AF optimised in terms of patient compliance? Question 6b – Is the current clinical pathway for AF optimised in terms of prescribing patterns for anticoagulants?	6a. Das 2015 [31]; Hodgkinson 2011 [32]; Johnson 2016 [33]; Martinez 2016 [34]; Mueller 2017 [35]. 6b. Corteville 2015 [36];Das 2015 [31]; Induruwa 2017 [37]; Isaew 2017 [38]; Gallager 2014 [39]; Kerr 2014 [40]; Lonsdale 2016 [41]; Martinez 2016 [34]; Mazurek 2017 [42]; NHS Blackpool; Quality and Outcomes Framework (QOF) [43-46]).

AF – atrial fibrillation

Methods

The current review was conducted by YHEC, in keeping with the UK NSC evidence review process. Database searches were conducted from 8 January 2018 to 3 March 2018 to identify studies relevant to the questions detailed in Table 1.

Eligibility for inclusion in the review

The following review process was followed:

1. Each abstract was reviewed against the inclusion/exclusion criteria by two reviewers. Where the applicability of the inclusion criteria was unclear, the article was included at this stage in order to ensure that all potentially relevant studies were captured. Any disagreements were resolved by discussion until a consensus was met.
2. Full-text articles required for the full-text review stage were acquired.
3. Each full-text article was reviewed against the inclusion/exclusion criteria by two reviewers, who determined whether the article was relevant to one or

more of the review questions. Any disagreements were resolved by discussion until a consensus was met.

Eligibility criteria for each question are presented inTable 2.

Table 2. Inclusion and exclusion criteria for the key questions

Key questions	Inclusion criteria				
	Population	**Intervention and comparator**	**Outcome**	**Study type**	Limits/exclusions
1a. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF? 1b. Is the risk of stroke similar between people with asymptomatic compared to symptomatic AF?	For question 1a, eligible studies had to compare the following population groups: • Adults with paroxysmal AF to • Adults with persistent AF or adults with permanent AF. For question 1b, eligible studies had to compare: • Adults with asymptomatic AF to • Adults with symptomatic AF.	For these questions, there were no interventions or comparators of interest (i.e. this question only addresses risk factors of stroke in adults with different types of AF).	Studies were included that evaluated one or more of the following outcomes: • Stroke; • Stroke risk; • Stroke mortality. When reported in any of the included studies, we aimed to stratify the outcomes by patient age.	For this question, we prioritised systematic reviews of case control and cohort studies, but none were identified[1]. Therefore we further identified any relevant case control studies, comparative cohort studies, and subgroup analyses reported in RCTs.	Only publications dated from January 2011 onwards were included in the review. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

[1] A systematic review by Welton [26] reported some data relevant to question 1a and 1b, but this was incorportated in a section on 'methods for the economic evaluation of AF screening' and was used to inform an economic model. This was not consided to be full systematic review evidence.

Question 2a – What is the benefit of treating screen-detected AF? Question 2b – Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?	For question 2a, eligible studies had to assess: • Adults >65 years of age with screen detected AF who received treatment compared to; • Adults >65 years of age with screen detected AF who did not receive treatment. For question 2b, eligible studies had to assess: • Formal screening programmes for AF in adults >65 years (any type of screening strategy) followed by treatment compared to; • Routine clinical diagnosis of AF in adults >65 years (presentation with symptoms) followed by treatment.	For question 2a, eligible studies had to compare anticoagulation treatment for the prevention of stroke versus no anticoagulation treatment. A comparator was not relevant for question 2b. For both questions, eligible anticoagulant treatments included: • Apixaban; • Dabigatran etexilate; • Edoxaban; • Rivaroxaban; • Vitamin K-antagonists (warfarin, acenocoumarol and phenindione only); • Heparin (heparin, dalteparin sodium, enoxaparin sodium, and tinzaparin sodium only).	Eligible studies had to evaluate one or more of the following outcomes: • Stroke; • Stroke risk; • Stroke mortality; • All-cause mortality; • Thromboembolic events; • Congestive heart failure; • Cognitive dysfunction; • Quality of Life; • Improvement of symptoms/episodes of AF; • Adverse effects/ Unintended consequences of oral anticoagulants. When reported in any of included studies, we also planned to stratify the outcomes by patient age.	The following study designs were prioritised: systematic reviews of RCTs, case control, and comparative cohort studies. We also attempted to find relevant case control studies, and comparative cohort studies, but none were identified.	Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

	Population	Screening test and tester	Reference test and tester	Outcome	Study type	Limits/exclusions
Question 3 – What is the reported accuracy of screening tests for all types of AF?	For this question, eligible studies had to assess adults >65 years of age.	Studies were eligible for inclusion if they investigated the accuracy of a single screening test for AF or a combination of screening tests, recording which health professional conducts the screening test.	Studies were eligible for inclusion if they compared the index test to the reference test (12-lead ECG performed and read by a cardiologist).	Measures of diagnostic accuracy of the screening test included: • Sensitivity; • Specificity; • Positive predictive value /Negative predictive value. When possible, we planned to conduct sub-group analyses by the type of healthcare professional who interpreted the test. We also planned to stratify the outcomes by patient age and type of AF detected.	We prioritised systematic reviews of diagnostic test accuracy studies. In addition, we included individual diagnostic test accuracy studies (consecutively enrolled populations) that post-dated any relevant systematic reviews.	Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.
	Population	**Intervention and comparator**		**Outcome**	**Study type**	**Limits/exclusions**
Question 4 – Have randomised controlled trials (RCTs)	For this question, eligible studies had to assess adults >65 years of age	Studies were included that compared formal screening programmes for AF in adults >65 years (any type		We include studies that evaluated one or more of the following outcomes:	For this question, systematic reviews of RCTs were prioritised, followed by RCTs.	Only publications dated from January 2011 onwards were

demonstrated a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?		of screening strategy) versus routine clinical diagnosis of AF (presentation with symptoms). Where possible, we aimed to report data on the frequency and interval of screening.	• Stroke; • Stroke risk; • Stroke mortality; • All-cause mortality; • Cardiovascular events; • Thromboembolic events; • Congestive heart failure; • Cognitive dysfunction; • QoL; • Improvement of symptoms/episodes of AF; • Incidental outcomes e.g. atrial flutter; • Adverse effects; • Harms of screening. When reported in any of included studies, we planned to stratify outcomes by patient age.		included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.
Question 5 – Is screening for AF in adults cost-effective?	For this question, eligible studies had to assess adults >65 years of age.	Studies were included that compared formal screening programmes for AF in adults >65 years (any type of screening strategy) versus routine clinical diagnosis of AF (i.e. identification of AF by a health care professional during a routine clinical appointment rather than as	For this question, eligible studies had to evaluate: • Cost-effectiveness measured using quality adjusted life years	Eligible designs were: • Systematic reviews of cost-utility analyses; • Health technology assessments; • Cost-utility analyses; • Economic models.	Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference

		part of a formal screening programme).		When reported in any of included studies, we planned to stratify outcomes by patient age. We also planned to capture data on frequency and interval of screening, and length of screening, if reported in the included studies.	abstracts were excluded.
Question 6a – Is the current clinical pathway for AF optimised in terms of patient compliance? Question 6b – Is the current clinical pathway for AF optimised in terms of prescribing patterns for anticoagulants?	For question 6a, eligible studies had to assess adults with AF taking anticoagulants. For question 6b, eligible studies had to assess prescribers of anticoagulants for patients with AF.	Anticoagulant treatments of interest included: • Apixaban; • Dabigatran etexilate; • Edoxaban; • Rivaroxaban; • Vitamin K-antagonists (warfarin, acenocoumarol and phenindione only); • Heparin (heparin, dalteparin sodium, enoxaparin sodium and tinzaparin sodium only).	For question 6a, eligible studies had to evaluate patients' compliance/adherence to anticoagulants. For question 6b, eligible studies had to evaluate prescribing patterns for anticoagulants.	For this question, eligible study designs were: • Observational cohort studies; • Epidemiological studies; • Record linkage studies and audits; • Quality and outcomes framework data.	Only publications dated from January 2011 onwards, and studies conducted in the UK, were included. Conference abstracts were excluded.

AF- atrial fibrillation; ECG – electrocardiogram; RCT – randomised controlled trial

Data extraction

A single researcher extracted relevant studies with a sample (25%) checked by a second reviewer. Any disagreements were resolved through discussion or by consulting a third reviewer.

Appraisal for quality/risk of bias tool

The following tools were used to assess the quality and risk of bias of each study included in the review:

- systematic reviews: A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2) [47]
- RCTs: Cochrane's "Risk of Bias" Tool [48]
- diagnostic accuracy studies: Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [49]
- case control studies: Centre for Review's and Dissemination (CRD) Case control checklist [50]
- cohort studies: Critical Appraisal Skills Programme (CASP) Cohort Study Checklist [51]
- economic evaluations: Checklist specified in National Institute for Health and Care Excellence (NICE) single technology appraisal (STA) guidance, adapted from Drummond (1996) [52]

Databases/sources searched

The literature search was undertaken in the resources listed in Table 3.

Table 3. Databases/sources searched

Resource	Interface / URL	Coverage dates	Date of search
Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)	Ovid SP	1946 to present	20 Feb 2018 and 22 Feb 2018
Embase	OvidSP	1974 to 20 Feb 2018	21 Feb 2018 and 22 Feb 2018 and 1 March 2018
Database of Abstracts of Reviews of Effects	Cochrane Library / Wiley	All available records	21 Feb 2018 and 23 Feb 2018 and 1 March 2018
Health Technology Assessment Database	Cochrane Library / Wiley	All available records	21 Feb 2018 and 23 Feb 2018 and 1 March 2018
Cochrane Database of Systematic Reviews	Cochrane Library / Wiley	Issue 2 (Feb 2018)	21 Feb 2018 and 23 Feb 2018 and 1 March 2018

Resource	Interface / URL	Coverage dates	Date of search
Cochrane Central Register of Controlled Trials (searches 2 and 3 only)	Cochrane Library / Wiley	(a) Issue 1 (Jan 2018) (b) Issue 2 (Feb 2018)	(a) 23 Feb 2018 (b) 1 March 2018
NHS Economic Evaluation Database (search 2 only)	Cochrane Library / Wiley	All available records	23 Feb 2018
Cost-Effectiveness Analysis (CEA) Registry (search 2 only)	http://healtheconomics.tuftsmedicalcenter.org/cear4/home.aspx	All available records	23 Feb 2018
Google (search 3 only)	https://www.google.co.uk/	N/A	2 March 2018

Three separate literature searches were undertaken to identify relevant studies for the 6 research questions (see Appendix 1). The development of search strategies and the conduct of searches reflected PHE guidance on conducting literature searches to inform evidence summaries[2]. The literature search process took a systematic approach, aiming to identify the relevant published literature based on the agreed questions.

Strategies excluded animal studies using a standard algorithm. Strategies were restricted to studies published in English language from 2011 to date. The strategies also excluded some publication types which were unlikely to yield relevant study reports (editorials, news items and case reports) and records with the phrase 'case report' in the title.

Where geographical limits were applied, searches were limited to Europe, United States, Canada, Australia and 6 where the search was restricted to UK studies only. Search terms for the UK context were based on the strategy developed by the National Institute for Health and Care Excellence (NICE) to retrieve research in Ovid MEDLINE about the UK [53].

Where a search included terms for comparative observational studies, the terms used drew on the strategy developed by the Scottish Intercollegiate Guidelines Network (SIGN) to identify observational studies[3], with the SIGN strategy focused in a highly pragmatic way to target records which made the comparative context explicit.

Where possible, we downloaded the results of searches in a tagged format and loaded them into bibliographic software (EndNote) [54]. Results from all

[2]Guidance Appendix G: Literature searches for evidence summaries. 2016. https://www.gov.uk/government/publications/uk-nsc-evidence-review-process/appendix-g-literature-searches-for-evidence-summaries

[3] http://www.sign.ac.uk/search-filters.html

3 searches were imported into a single EndNote Library and deduplicated using several algorithms. Duplicate references were held in a separate EndNote database for checking if required. Results from resources which did not allow export in a format compatible with EndNote were saved in a Word document and manually deduplicated.

Across all 3 searches 10,389 records were identified (Table 3). Following deduplication 5859 records were assessed for relevance.

Table 3. Database search results

Resource	Number of records identified (search 1)	Number of records identified (search 2)	Number of records identified (search 3)	Total number of records identified across all 3 searches
Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R)	1235	792	1946	3973
Embase	889	644	2789	4322
Database of Abstracts of Reviews of Effects	38	12	44	94
Health Technology Assessment Database	6	7	16	29
Cochrane Database of Systematic Reviews	19	2	9	30
Cochrane Central Register of Controlled Trials (searches 2 and 3 only)	n/a	553	1256	1809
NHS Economic Evaluation Database (search 2 only)	n/a	7	0	7
Cost-Effectiveness Analysis (CEA) Registry (search 2 only)	n/a	102	0	102
Google (search 3 only)	n/a	n/a	23	23
Total number of records retrieved	2187	2119	6083	10389
Total number of records after deduplication		25		5859

The included study references in the following systematic review article were checked against the search results to identify any further relevant studies:

- Welton NJ, McAleenan A, Thom HHZ, Davies P, Hollingworth W, Higgins JPT, et al. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis. Health Technol Assess 2017;21(29)

Two studies were absent from our library but were not added for assessment as these were published prior to the date limit of January 2011.

Question level synthesis

Question 1 Criterion 1

The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.

Question 1a – Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF?

Question 1b – Is the risk of stroke similar between people with asymptomatic compared to symptomatic AF?

Eligibility for inclusion in the review

The eligibility criteria according to population, intervention, comparator, outcome and study design (PICOS) are described in this section.

Population

For question 1a, eligible studies had to compare the following population groups:

- adults with paroxysmal AF to
- adults with persistent AF or adults with permanent AF

Briefly, paroxysmal AF, also referred to as intermittent AF, is defined as an AF episode that terminates spontaneously or following intervention within seven days, and where episodes may recur with variable frequency [55].

Persistent AF is defined as continuous AF that is sustained for more than seven days and long-term persistent AF is defined as continuous AF lasting more than 12 months. Permanent AF is a term used when the patient and clinician decide together to discontinue further attempts to restore and/or maintain sinus rhythm [55].

For question 1b, eligible studies were required to compare:

- adults with asymptomatic AF to
- adults with symptomatic AF

Asymptomatic AF, also referred to as silent AF, occurs when patients have AF, but are not aware that they are experiencing AF. It may manifest as an AF-related complication (e.g. ischaemic stroke or tachycardiomyopathy) or may be diagnosed by an opportunistic electrocardiogram. Silent AF may present as any of the temporal forms of AF (i.e. paroxysmal, persistent, permanent, etc.) [56]. Conversely, symptomatic patients will be aware they have one of the types of AF.

Intervention and comparator

For these questions, there were no interventions or comparators of interest (i.e. this question only addresses risk of stroke in adults with different types of AF).

Outcomes

Studies were included that evaluated one or more of the following outcomes:

- stroke
- stroke risk
- stroke mortality

When reported in any of the included studies, we aimed to stratify the outcomes by patient age.

Study types

For this question, we prioritised systematic reviews of case control and cohort studies, but none were identified. Therefore we further identified any relevant case control studies, comparative cohort studies, and subgroup analyses reported in RCTs.

Limits

Only publications dated from January 2011 onwards were included in the review. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, of which ten studies (in 11 publications) were judged to be relevant to this criterion. An additional relevant article (Vanassche 2015) was identified through hand-searching reference lists, resulting in 11 studies (reported in 12 publications) that addressed these review questions; nine studies addressed question 1a and two studies addressed question 1b.

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

Question 1a: paroxysmal AF vs. persistent or permanent AF

Nine studies (reported in ten publications) presented comparative data for patients with paroxysmal AF compared with patients who had persistent or permanent AF (Al-Khatib 2013; Banerjee 2013; Baturova 2014; Disertori 2013; Flaker 2012; Lip 2014; Meinertz 2011; Proietti 2017; Steinberg 2015; Vanassche 2015) [10-13, 20]. One of the included studies was a case-control study (Baturova 2014) [12], three were comparative cohort studies (Banerjee 2013; Lip 2014; Proietti 2017 [Lip and Proietti are the same study]; Meinertz 2011) [11, 15-18] and five were subgroup analyses of RCTs (Al-Kahib 2013; Disertori 2013; Flaker 2012; Steinberg 2015; Vanassche 2015) [10, 13, 14, 19, 20]. None of these studies stratified outcomes by patient age. Details of these studies are summarised narratively below and in Appendix 3, Tables 3.1 and 3.2.

The majority of studies reported that patients with persistent AF or permanent AF were more likely to be male and were significantly older than patients with paroxysmal AF. The exceptions to this were that no differences in age were found between patients with paroxysmal and persistent AF in the study by Banerjee (2013) [11] (although there was a significant difference between patients with paroxysmal and permanent AF as above), and no significant difference in the proportions of males was observed in patients with different types of AF in the studies by Lip (2014) [15, 16] and Proietti (2017) [18]. Further baseline differences between the groups were often reported in terms of comorbidities, but consideration of these comparisons and their potential impact on the outcomes is beyond the remit of this NSC rapid review if not already considered by the study authors. As reported above, this question aimed to address whether or not there were differences between the types of AF on stroke, stroke risk, and stroke mortality.

Stroke

Seven studies (reported in eight publications) presented comparative stroke data for patients with paroxysmal AF versus persistent or permanent AF (Al-Khatib 2013; Banerjee 2013; Disertori 2013; Flaker 2012; Lip 2014; Proietti 2017; Steinberg 2015; Vanassche 2015) [10, 11, 13-16, 18-20]. For this outcome, the studies reported on: stroke, ischaemic stroke, thromboembolic events, or stroke and systematic embolism (together). One study only reported on readmissions for stroke (Lip 2014; Proietti 2017) [15, 16, 18]. We extracted data on all of these outcomes for comprehensiveness.

Overall, we found consistent evidence across several studies that the number of stroke events is significantly higher in patients with permanent AF compared with patients who have paroxysmal AF. Differences between persistent and paroxysmal AF are less consistent. These findings were limited because not all studies were analysed using the same methods; some studies reported unadjusted hazard ratios (HRs) while others reported adjusted HRs. These differences may limit comparability between studies where baseline populations were not similar. For example, Banerjee (2013) [11] reported that rates of stroke differed between different types of AF, but in multivariate analyses, they found that other baseline factors (e.g. previous stroke, age, heart failure and vascular disease) independently increased risk of adverse events including stroke.

The detailed results are as follows and in Table 5:

- two studies that reported subgroup data from RCTs found significantly higher **stroke event rates** in patients with persistent AF or permanent AF compared with paroxysmal AF patients

    1. Steinberg (2015) [19] (n=14,062) compared paroxysmal vs. permanent AF events per 100 patient-years: Adjusted[4] HR: 0.78 (95% CI: 0.61, 0.99), p=0.045.
    2. Vanassche (2015) [20] (n=6,573) compared patients with paroxysmal vs. persistent or permanent AF percentage per year: Adjusted HR: 1.44 (95% CI: 1.05, 1.98), p=0.02 (persistent AF) and Adjusted[5] HR: 1.83 (95% CI: 1.43, 2.35), p<0.001 (permanent AF).

[4] Adjusted for the following (at baseline): age, sex, body mass index (BMI), region, diabetes, prior stroke/TIA, vascular disease [myocardial infarction (MI), peripheral artery disease (PAD), carotid occlusive disease], CHF, hypertension, chronic obstructive pulmonary disease, diastolic blood pressure (BP), creatinine clearance ,12 heart rate, and abstinence from alcohol.
[5] Adjusted for age ≥ 75 years, sex, prior stroke or TIA, hypertension, diabetes, heart failure, peripheral arterial disease, and stroke risk (categorised CHA_2DS_2-VASc score).

- one retrospective cohort study (n=7,156) reported that ischaemic stroke event rates per 100 person-years were significantly higher in patients with permanent AF compared to patients with paroxysmal AF (0.59 vs. 0.46, p=0.01); no differences were reported between patients with persistent and paroxysmal AF (0.45 vs. 0.46, p=0.54) (Banerjee 2013) [11]

- one subgroup analysis of a RCT (n=1,442) reported no significant difference in **thromboembolic events** in patients with persistent AF compared with patients with paroxysmal AF: Adjusted[6] HR: 2.14 (95% CI: 0.68, 6.79), p=0.20 (Disertori 2013) [13]
- three studies reported significantly higher event rates of **stroke and systemic embolism (or thromboembolism)** in patients with permanent AF compared with paroxysmal AF patients, but one study reported similar percentages between these patients. Differences were not consistent in comparisons of patients with persistent vs. paroxysmal AF

    1. Al-Khatib (2013) [10] (n=18,201) (a subgroup analysis of a RCT) compared paroxysmal vs. persistent or permanent AF on the number of stroke or systemic embolism events per 100 patient-years. Rates were 0.98 with paroxysmal AF and 1.52 with persistent or permanent AF (Unadjusted HR: 0.65 (95% CI: 0.48, 0.87), p=0.003).
    2. Banerjee (2013) [11] (n=7,156) (a retrospective cohort) compared paroxysmal vs. persistent, and paroxysmal vs. permanent AF stroke or thromboembolism events per 100 patient-years: 0.69 vs. 0.69, p=0.52 (paroxysmal AF vs. persistent AF) and 0.69 vs. 0.89, p=0.001 (paroxysmal AF vs. permanent AF) (hazard ratios not reported).
    3. Flaker (2012) [14] (n=18,107) (a subgroup analysis of a RCT) reported data on paroxysmal, persistent, and permanent AF rates per year (1.32%, 1.55% and 1.49% respectively), but no statistical comparisons were reported.

- one prospective cohort study (n=2,589) reported on **readmissions for stroke** at one (Lip 2014) [16, 57] and two years (Proietti 2017) [18] in patients with paroxysmal AF, persistent AF, long-standing persistent AF, and permanent AF. The data in these publications, however, are difficult to interpret because overall event rates for the population groups are not presented. The authors did compare the number of readmissions for stroke using a denominator of readmissions for all types of cardiovascular events within each group. The percentages between groups were similar between patients with different types of AF (p=0.945 for among-group comparisons at 1 year and p=0.687 at 2 years)

[6] Adjusted for warfarin treatment and $CHADS_2$ score.

Table 5. Studies relevant to criterion 1 (question 1a): stroke

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke
Al-Khatib 2013 [10] Subgroup analysis from a RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2786/18201 (15.3%)	Paroxysmal AF was defined as recurrent AF that terminates spontaneously, persistent AF was defined as AF that is sustained beyond 7 days, and permanent AF was defined as long-standing AF in which restoring and/or maintaining sinus rhythm has failed or has been foregone.	Median age (25th, 75th): 69 (61, 75) years % male: 58%	**Stroke or systematic embolism** number of events (%/100 patient years): 51 (1.0%)
	Persistent or permanent AF: n/N=15412/18201 (84.7%)		Median age (25th, 75th): 70 (63, 76) years, p<0.001 % male: 66%, p<0.001	**Stroke or systematic embolism** number of events (%/100 patient years): 426 (1.5%) Unadjusted HR: 0.65 (95% CI: 0.48, 0.87), p=0.003
Banerjee 2013 [11] Retrospective cohort *(data collected between 2000 and 2010)*	Paroxysmal AF: n/N=4176/7156 (58.4%)	Paroxysmal NVAF was defined as self-terminating episodes of AF (usually within 7 days), whilst persistent NVAF is present when an NVAF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion; long-standing persistent NVAF has lasted for ≥1 year when it is decided to adopt a rhythm control strategy. Permanent NVAF exists when the presence of the arrhythmia is accepted by the patient (and physician) and it has been present for ≥1 year.	Mean age: 68.0 (SD 16.2) years % male: 58%	**Ischaemic stroke** events/event rate: 192, 0.46 (0.40, 0.53) **Stroke/TE** events/event rate: 287, 0.69 (0.61, 0.77)
	Persistent AF: n/N=376/7156 (5.3%)		Mean age: 67.4 (SD 12.1) years, p=0.98 (compared with paroxysmal) % male: 70%, p<0.001	**Ischaemic stroke** events/event rate: 17, 0.45 (0.26, 0.72), (p=0.54 compared with paroxysmal, HR not reported) **Stroke/TE** events/event rate: 26, 0.69 (0.45, 1.01), (p=0.52 compared with paroxysmal, HR not reported)
	Permanent AF: n/N=2604/7156 (36.3%)		Mean age: 73.7 (SD 12.9) years p<0.001 (compared with paroxysmal) % male: 68%, p<0.001	**Ischaemic stroke** events/event rate: 153, 0.59 (0.5, 0.69), (p=0.01 compared with paroxysmal, HR not reported) **Stroke/TE** events/event rate: 26, 0.89 (0.78, 1.01), (p=0.001

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke
				compared with paroxysmal, HR not reported)
Baturova 2014 [12] Case-control (*subgroup data extracted in patients with AF*) (*data from a cohort of stroke patients so no follow-up)*	Non-permanent AF: n/N = 100/153 (65.4%) Permanent AF: n/N = 53/153 (34.6%)	AF was defined as non-permanent when it was considered paroxysmal or persistent (with consecutive cardioversion) by the attending physician or when spontaneous conversion to sinus rhythm was proven by the ECG with sinus rhythm at inclusion. Patients who had AF diagnosis in the Swedish Hospital Discharge Register and had sinus rhythm at admission were considered having non-permanent AF. Permanent AF was diagnosed in accordance with documentation in medical records, or when serial ECGs demonstrated arrhythmia without intervening sinus rhythm, including admission ECG.	M Median age: 80 (IQ 13) years *(no other baseline characteristics reported for the subgroup of patients with AF)* Median age: 84 (IQ 10) years, p=0.002	Stroke data not reported as all patients has a stroke at baseline. The authors only presented information on stroke severity measured by the NIHSS scale: Non-permanent median score 5 (IQ 12) vs permanent median score 4 (IQ 11), p=0.941
Disertori 2013 [13] Subgroup analysis from a RCT (*1 year follow-up)*	Paroxysmal AF: n/N=771/1442 (53.5%) Persistent AF: n/N=463/1442 (32.1%) *Categorisation was not made in the remaining 14.4% of patients*	AF was defined as paroxysmal if the AF was self-terminating, usually within 48 hours, although AF could continue for up to 7 days; AF was defined as persistent when the AF episodes lasted longer than 7 days. Arrhythmia termination by cardioversion did not change the classification of AF.	Mean age: 66.8 (SD 9.8) years % male: 55% Mean age: 68.8 (SD 8.5) years, p=0.0002 % male: 71%, p<0.0001	**Thromboembolic events** 6 (0.8%) **Thromboembolic events** 6 (1.3%) Adjusted HR 2.14 (95% CI: 0.68, 6.79), p=0.20

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke
Flaker 2012 [14] Subgroup analysis from a RCT (*mean follow-up 2 years)*	Paroxysmal AF: n/N=5943/18107 (32.8%)	Not reported	Not reported by type of AF	**Stroke or systemic embolism** 1.32% per year
	Persistent AF: n/N=5789/18107 (32.0%)			**Stroke or systemic embolism** 1.55% per year
	Permanent AF: n/N=6375/18107 (35.2%)			**Stroke or systemic embolism** 1.49% per year (*no statistical comparisons were reported*)
Lip 2014 (*1 year follow-up*); Proietti 2017 [18] *(2 year follow-up)* Prospective cohort *(up to 2 years follow-up)*	Paroxysmal AF: n/N=693/2589 (26.8%)	Not reported	Mean age: 66.7 years (SD 11.4) % male: 58%	**Readmissions for stroke** 1 year: 2/627 2 years: 1/495 (*denominators are not clear – we have extracted data on what appears to be the total number of readmissions within each group*)
	Persistent AF: n/N=550/2589 (21.2%)		Mean age: 67.9 years (SD 11.0) % male: 60%	**Readmissions for stroke** 1 year: 2/477 2 years: 0/363
	Long-standing persistent AF: n/N=121/2589 (4.7%)		Mean age: 70.9 years (SD 10.8) % male: 61%	**Readmissions for stroke** 1 year: 0/73 2 years: 0/82
	Permanent AF: n/N=451/ 2589 (17.4%)		Mean age: 73.0 years (SD 10.2) % male: 58%	**Readmissions for stroke** 1 year: 4/382 2 years: 5/309
Steinberg 2015 [19] Subgroup *post hoc* analysis from RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2514/14 062 (17.9%)	Patients experiencing episodic AF, self-terminating within 7 days, are said to have paroxysmal AF; patients whose arrhythmia persists beyond 7 days (or requires intervention to terminate) are considered to have persistent	Median age: 72 (25^{th}, 75^{th} percentile: 65, 78) years % male: 55%	**Stroke** Events/100 patient years (total events): 1.59 (78)
	Persistent AF: n/N=11548/14 062 (82.1%)		Median age: 73 (25^{th}, 75^{th} percentile: 65, 78) years, p=0.033 % male 61%, p<0.001	**Stroke** 2.02 (446) Adjusted HR: 0.78 (95% CI 0.61, 0.99), p=0.045

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke
		AF.		
Vanassche 2015 [20] (*subgroup analysis from two double-blind, placebo controlled RCTs*) *Data on follow-up NR*	Paroxysmal AF: n/N=1576/6573 (24%)	Paroxysmal AF episodes are self-limiting and shorter than 1 week, episodes lasting longer than 7 days are referred to as persistent, and permanent AF refers to AF without any intercurring sinus rhythm.	Mean age: 69.0 (± 9.9) years % male: 52.3%	**Stroke** No, of events/patient: 77/1576 Event rate %/year: 2.1%
	Persistent AF: n/N=1136/6573 (17%)		Mean age: 68.6 (± 10.2) years % male: 57.7%	**Stroke** No, of events/patient: 74/1136 Event rate %/year: 3.0% Adjusted HR 1.44 (95% CI; 1.05, 1.98), p=0.02
	Permanent AF: n/N=3854/6573 (59%)		Mean age: 71.9 (± 9.8) years, p<0.001 % male: 60.2%, p<0.001	**Stroke** No, of events/patient: 385//3854 Event rate %/year: 4.2% Adjusted HR 1.83 (95% CI; 1.43, 2.35), p<0.001

AF: Atrial fibrillation; CI: Confidence interval; ECG: Electrocardiogram; HR: Hazard ratio; IQ: Interquartile range; NA: Not applicable; NIHSS: National Institutes of Health Stroke Scale; NR: Not reported; NVAF: Non-valvular atrial fibrillation; SD: Standard deviation; TE: Thromboembolism

Stroke risk

Eight studies (reported in nine publications) presented stroke risk data for patients with paroxysmal AF versus persistent or permanent AF (Al-Khatib 2013; Banerjee 2013; Baturova 2014; Disertori 2013; Lip 2014; Meinertz 2011; Proietti 2017; Steinberg 2015; Vanassche 2015) [10-13, 15-20]. Stroke risk was reported using CHADS2 and/or CHA2DS2-VASc scores. These scores were reported as a mean, median, or categorised (with scores of 2 or greater indicating a higher risk of stroke). In all of the studies, this information was extracted from patient characteristics at baseline.

Overall, the studies reported consistent evidence that mean CHADS2 and CHA2DS2-VASc scores were significantly higher in patients with permanent AF compared with patients with paroxysmal AF. Similarly, the percentages of patients with CHADS2 and CHA2DS2-VASc scores ≥2 (indicating high risk of stroke) were consistently higher in patients with permanent AF. For all outcome measures, differences between persistent AF and paroxysmal AF were less consistent.

The detailed results are as follows and in Table 6:

- four studies reported on mean CHADS2 scores (Al-Khatib 2013; Meinertz 2011; Steinberg 2015; Vanassche 2015) [10, 17, 19, 20]
    1. Al-Khatib (2013) [10] combined data for patients with persistent and permanent AF. In this combined group the mean CHADS2 score was 2.1 (SD 1.1), which was significantly higher than those with paroxysmal AF (2.0 [SD1.1] $p<0.001$)[7].
    2. Two studies presented data for all three types of AF and both reported significantly higher mean scores in patients with permanent AF:
        a. Meinertz 2011 [17]: permanent AF: 2.4 [SD 4.1]; persistent AF: 2.1 [SD 1.2]; paroxysmal AF: 1.9 [SD 1.2]: $p<0.0001$.

        b. Vanassche 2015 [20]: permanent AF: 3.6 [SD 1.5]; persistent AF: 3.1 [SD 1.4]; paroxysmal AF: 3.1 [SD 1.4]: $p<0.001$).

    3. One study only compared means in paroxysmal AF versus persistent AF patients and reported that both groups had the same score (3.5 [SD 1.3]) (Steinberg 2015) [19].

[7] Data and significance value as reported by study authors, although values in groups appear similar.

- one study reported that median CHADS2 scores were significantly higher in patients with permanent AF compared with patients with non-permanent AF (2 (IQ 3) vs. 2 (IQ 2), p=0.039[8]) (Baturova 2014) [12]
- two studies reported mean CHA2DS2-VASc scores (Meinertz 2011; Steinberg 2015) [17, 19]. Meinertz (2011) [17] presented data for all three types of AF, and across all groups, reported significantly higher scores in those with permanent AF (4.1 [1.7]) compared with those with persistent AF (3.7 [SD 1.6]) or paroxysmal AF: 3.4 [SD 1.7]: p<0.0001). Steinberg (2015) [19] compared means among patients with paroxysmal AF versus persistent AF patients and reported that both groups had the same mean score (4.9 [1.3])
- two studies reported on the percentage of patients with a CHADS2 score ≥2 (Banerjee 2013; Disertori 2013) [11, 13]. Neither study reported differences between those with paroxysmal versus persistent AF (Banerjee 2013: 50% vs. 48%, p=0.70; Disertori 2013 [13]: 35% vs. 38%, p=0.40), however, Banerjee (2013) [11] reported that a significantly higher percentage of patients with permanent AF had a score ≥2 compared to those with paroxysmal AF (60% vs. 50%, p=0.008). Disertori (2013) [13] did not assess permanent AF
- three studies (reported in four papers) reported on the percentage of patients with a CHA2DS2-VASc score ≥2 (Banerjee 2013; Lip 2014; Proietti 2017; Vanassche 2015) [11, 15, 16, 18, 20]. One study reported significantly higher percentages of patients with scores ≥2 in those with persistent AF compared with paroxysmal AF (Banerjee 2013: 76% vs. 74%, p=0.049), and also in those with permanent AF compared with paroxysmal AF (Banerjee 2013 [11]: 85% vs. 74%, p=0.02). A second study found similar percentages of high risk patients in patients with paroxysmal and persistent AF (87% vs. 86%), although a significantly higher percentage with permanent AF had scores ≥2 compared with patients with paroxysmal AF (93% vs. 87%, p<0.001). Although percentages increased by type of AF in Lip (2014) and Proietti (2017) [18] (73%, 81% and 92%), statistical comparisons were not reported

[8] Data and significance value as reported by study authors, although values in groups appear similar.
[9] Data and significance value as reported by study authors, although values in groups appear similar.

Table 6. Studies relevant to criterion 1 (question 1a): stroke risk

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke risk
Al-Khatib 2013 [10] Subgroup analysis from a RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2786/18201 (15.3%) Persistent or permanent AF: n/N=15412/18201 (84.7%)	Paroxysmal AF was defined as recurrent AF that terminates spontaneously, persistent AF was defined as AF that is sustained beyond 7 days, and permanent AF was defined as long-standing AF in which restoring and/or maintaining sinus rhythm has failed or has been foregone.	Median age (25^{th}, 75^{th}): 69 (61, 75) years % male: 58% Median age (25^{th}, 75^{th}): 70 (63, 76) years, p<0.001 % male: 66%, p<0.001	Mean $CHADS_2$ score: 2.0 (SD1.1) Mean $CHADS_2$ score: 2.1 (SD 1.1), p<0.001
Banerjee 2013 [11] Retrospective cohort *(data collected between 2000 and 2010)*	Paroxysmal AF: n/N=4176/7156 (58.4%) Persistent AF: n/N=376/7156 (5.3%) Permanent AF: n/N=2604/7156 (36.3%)	Paroxysmal NVAF was defined as self-terminating episodes of AF (usually within 7 days), whilst persistent NVAF is present when an NVAF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion; long-standing persistent NVAF has lasted for ≥1 year when it is decided to adopt a rhythm control strategy. Permanent NVAF exists when the presence of the arrhythmia is accepted by the patient (and physician) and it has been present for ≥1 year.	Mean age: 68.0 (SD 16.2) years % male: 58% Mean age: 67.4 (SD 12.1) years, p=0.98 (compared with paroxysmal) % male: 70%, p<0.001 Mean age: 73.7 (SD 12.9) years p<0.001 (compared with paroxysmal) % male: 68%, p<0.001	% with $CHADS_2$ score ≥2: 2080 (49.8%) % with CHA_2DS_2-VAS_C score ≥2 (high risk): 3080 (73.7%) % with $CHADS_2$ score ≥2: 181 (48.1%), p=0.70 (compared with paroxysmal) % with CHA_2DS_2-VAS_C score ≥2 (high risk): 285 (75.8%), p=0.04 % with $CHADS_2$ score ≥2: 1556 (59.8%), p=0.008 (compared with paroxysmal) % with CHA_2DS_2-VAS_C score ≥2 (high risk): 2200 (84.5%), p=0.02
Baturova 2014 [12] Case-control (*subgroup data extracted in patients with AF*)	Non-permanent AF: n/N = 100/153 (65.4%)	AF was defined as non-permanent when it was considered paroxysmal or persistent (with consecutive cardioversion) by	M Median age: 80 (IQ 13) years *(no other baseline characteristics reported for the subgroup of patients with AF)*	Median $CHADS_2$ score: 2 (IQ 2)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke risk
(*data from a cohort of stroke patients so no follow-up)*	Permanent AF: n/N = 53/153 (34.6%)	the attending physician or when spontaneous conversion to sinus rhythm was proven by the ECG with sinus rhythm at inclusion. Patients who had AF diagnosis in the Swedish Hospital Discharge Register and had sinus rhythm at admission were considered having non-permanent AF. Permanent AF was diagnosed in accordance with documentation in medical records, or when serial ECGs demonstrated arrhythmia without intervening sinus rhythm, including admission ECG.	Median age: 84 (IQ 10) years, p=0.002	Median $CHADS_2$ score: 2 (IQ 3), p=0.039
Disertori 2013 [13] Subgroup analysis from a RCT (*1 year follow-up)*	Paroxysmal AF: n/N=771/1442 (53.5%)	AF was defined as paroxysmal if the AF was self-terminating, usually within 48 hours, although AF could continue for up to 7 days; AF was defined as persistent when the AF episodes lasted longer than 7 days. Arrhythmia termination by cardioversion did not change the classification of AF.	Mean age: 66.8 (SD 9.8) years % male: 55%	% with $CHADS_2$ score ≥2: 268 (34.8%)
	Persistent AF: n/N=463/1442 (32.1%) *Categorisation was not made in the remaining 14.4% of patients*		Mean age: 68.8 (SD 8.5) years, p=0.0002 % male: 71%, p<0.0001	% with $CHADS_2$ score ≥2: 174 (37.6%)
Lip 2014 (*1 year follow-up*); Proietti 2017 [18] *(2 year follow-up)* Prospective cohort *(up to 2 years follow-up)*	Paroxysmal AF: n/N=693/2589 (26.8%)	Not reported	Mean age: 66.7 years (SD 11.4) % male: 58%	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 506 (73.0%)
	Persistent AF: n/N=550/2589 (21.2%)		Mean age: 67.9 years (SD 11.0) % male: 60%	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 447 (81.3%)
	Long-standing persistent AF: n/N=121/2589 (4.7%)		Mean age: 70.9 years (SD 10.8) % male: 61%	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 107 (88.4%)
	Permanent AF: n/N=451/ 2589 (17.4%)		Mean age: 73.0 years (SD 10.2) % male: 58%	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 417 (92.5%)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke risk
Meinertz 2011 [17] Prospective cohort (*baseline data only*)	Paroxysmal AF: n/N=994/3667 (26%)	Not reported	Mean age: 69.8 (± 9.9) years % male: 56.8%	Mean $CHADS_2$ score: 1.9 (SD 1.2) Mean CHA_2DS_2-VAS_C score: 3.4 (SD 1.7)
	Persistent AF: n/N=944/3667 (27%)		Mean age: 71.4 (± 9.1) years % male: 59.7%	Mean $CHADS_2$ score: 2.1 (SD 1.2) Mean CHA_2DS_2-VAS_C score: 3.7 (SD 1.6)
	Permanent AF: n/N=1525/3667 (42%) (*non-specified in 6% patients*)		Mean age: 73.7 (± 8.4) years, p<0.0001 % male: 58.4%, p<0.0001	Mean $CHADS_2$ score: 2.4 (SD 1.3), p<0.0001 Mean CHA_2DS_2-VAS_C score: 4.1 (SD 1.7)), p<0.0001
Steinberg 2015 [19] Subgroup *post hoc* analysis from RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2514/14 062 (17.9%)	Patients experiencing episodic AF, self-terminating within 7 days, are said to have paroxysmal AF; patients whose arrhythmia persists beyond 7 days (or requires intervention to terminate) are considered to have persistent AF.	Median age: 72 (25^{th}, 75^{th} percentile: 65, 78) years % male: 55%	Mean $CHADS_2$ score: 3.5 (SD 0.9) Mean CHA_2DS_2-VAS_C score: 4.9 (SD 1.3)
	Persistent AF: n/N=11548/14 062 (82.1%)		Median age: 73 (25^{th}, 75^{th} percentile: 65, 78) years, p=0.033 % male 61%, p<0.001	Mean $CHADS_2$ score: 3.5 (SD 0.9), p=0.32 Mean CHA_2DS_2-VAS_C score: 4.9 (SD 1.3), p=0.07
Vanassche 2015 [20] (*subgroup analysis from two double-blind, placebo controlled RCTs*) *Data on follow-up NR*	Paroxysmal AF: n/N=1576/6573 (24%)	Paroxysmal AF episodes are self-limiting and shorter than 1 week, episodes lasting longer than 7 days are referred to as persistent, and permanent AF refers to AF without any intercurring sinus rhythm.	Mean age: 69.0 (± 9.9) years % male: 52.3%	Mean $CHADS_2$ score: 3.1 (SD 1.4) % Mean CHA_2DS_2-VAS_C score 2-3: 795 (50.5%) ≥4: 579 (36.8%)
	Persistent AF: n/N=1136/6573 (17%)		Mean age: 68.6 (± 10.2) years % male: 57.7%	Mean $CHADS_2$ score: 3.1 (SD 1.4) % Mean CHA_2DS_2-VAS_C score 2-3: 565 (49.7%) ≥4: 412 (36.3%)
	Permanent AF: n/N=3854/6573 (59%)		Mean age: 71.9 (± 9.8) years, p<0.001 % male: 60.2%, p<0.001	Mean $CHADS_2$ score: 3.6 (SD 1.5), p<0.001 % Mean CHA_2DS_2-VAS_C score 2-3: 1677 (43.5%)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke risk
				≥4: 1911 (49.6%), p<0.001

AF: Atrial fibrillation; CI: Confidence interval; ECG: Electrocardiogram; HR: Hazard ratio; IQ: Interquartile range; NA: Not applicable; NIHSS: National Institutes of Health Stroke Scale; NR: Not reported; NVAF: Non-valvular atrial fibrillation; SD: Standard deviation; TE: Thromboembolism

Stroke mortality

Only one of the included studies (in two publications) reported on ischaemic/haemorrhagic stroke deaths (Lip 2014; Proietti 2017) [16, 18]. In this prospective cohort study, there were 2/808 (0.24%)[10] stroke deaths in patients with paroxysmal AF, 1/647 (0.15%) in patients with persistent AF, and 1/526 (0.19%) in patients with permanent AF at one year follow-up. These figures have been calculated based on data presented in the papers, but no statistical comparisons were reported in this study for the groups of interest to this rapid review.

Four other studies reported on all-cause mortality (Al-Khatib 2013; Banerjee 2013; Disertori 2013; Steinberg 2015) [10, 11, 13, 19]. We briefly report these results although they are not a primary outcome of interest in this rapid review (with details in Table 7):

One subgroup analysis of a RCT found no significant difference in death rates between patients with persistent AF and patients with paroxysmal AF (0.65% vs. 1.2%; Adjusted HR 0.52 [95% CI: 0.13, 1.03], p=0.35) (Disertori 2013) [13], whereas a subgroup analysis of a second RCT found significantly higher rates (per 100 patient years) in patients with persistent AF compared to patients with paroxysmal AF (Adjusted HR 0.79 [95% CI: 0.67, 0.94], p=0.0061) (Steinberg 2015) [19]. A subgroup analysis of a third RCT also found a significantly higher event rate (per 100 patient years) in patients with persistent or permanent AF compared with patients with paroxysmal AF (Unadjusted HR 0.72 [95% CI: 0.61, 0.85], p=0.0002) (Al-Khatib 2013) [10]. A retrospective cohort did not observe any significant differences in event rates between patients with persistent AF and paroxysmal AF (1.14 vs. 0.99, p=0.20), but did observe a significant difference between patients with permanent AF and paroxysmal AF, with a higher death rate in patients with permanent AF (1.50 vs. 0.99, p<0.001) (Banerjee 2013).

[10]Percentages were calculated by review authors.

Risk of bias

Of the nine studies (reported in ten publications) that compared paroxysmal AF with persistent or permanent AF, five were subgroup analyses from RCTs of which two were explicitly reported as post hoc analyses (Disertori 2013; Steinberg 2015) [13, 19], one was a pre-specified analysis (Al-Khatib 2013) [10], and the remaining two did not report whether or not the analyses were post hoc (Flaker 2012; Vanassche 2015) [14, 20]. Although these trials were well conducted, any results from subgroup data should be considered as exploratory.

One case-control study reported subgroup data in patients with AF clinical types (Baturova 2014) [12]. Again, these subgroup analyses should be considered as exploratory.

The three remaining studies (in four publications) were cohort studies (Banerjee 2013; Lip 2014; Meinertz 2011; Proietti 2017) [11, 15-18]. One of the studies was limited in that only baseline data on stroke risk were presented so a full assessment of this study could not be made (Meinertz 2011) [17], and the other two studies appear to have been well conducted for this type of study.

A detailed critical appraisal for each included publication is presented in Appendix 3, Tables 3.16 to 3.18.

Table 7. Studies relevant to criterion 1 (question 1a): stroke mortality/mortality

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke mortality
Al-Khatib 2013 [10] Subgroup analysis from a RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2786/18201 (15.3%) Persistent or permanent AF: n/N=15412/18201 (84.7%)	Paroxysmal AF was defined as recurrent AF that terminates spontaneously, persistent AF was defined as AF that is sustained beyond 7 days, and permanent AF was defined as long-standing AF in which restoring and/or maintaining sinus rhythm has failed or has been foregone.	Median age (25th, 75th): 69 (61, 75) years % male: 58% Median age (25th, 75th): 70 (63, 76) years, p<0.001 % male: 66%, p<0.001	**All-cause mortality** number of events (%/100 patient years): 149 (2.8%) **All-cause mortality** number of events (%/100 patient years): 1123 (3.9%) Unadjusted HR: 0.72 (95% CI: 0.61, 0.85), p=0.0002

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke mortality
Banerjee 2013 [11] Retrospective cohort *(data collected between 2000 and 2010)*	Paroxysmal AF: n/N=4176/7156 (58.4%)	Paroxysmal NVAF was defined as self-terminating episodes of AF (usually within 7 days), whilst persistent NVAF is present when an NVAF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion; long-standing persistent NVAF has lasted for ≥1 year when it is decided to adopt a rhythm control strategy. Permanent NVAF exists when the presence of the arrhythmia is accepted by the patient (and physician) and it has been present for ≥1 year.	Mean age: 68.0 (SD 16.2) years % male: 58%	**All-cause mortality** events/event rate: 414, 0.99 (0.9, 1.09)
	Persistent AF: n/N=376/7156 (5.3%)		Mean age: 67.4 (SD 12.1) years, p=0.98 (compared with paroxysmal) % male: 70%, p<0.001	**All-cause mortality** events/event rate: 43, 1.14 (0.83, 1.54), (p=0.20 compared with paroxysmal)
	Permanent AF: n/N=2604/7156 (36.3%)		Mean age: 73.7 (SD 12.9) years p<0.001 (compared with paroxysmal) % male: 68%, p<0.001	**All-cause mortality** events/event rate: 390, 1.50 (1.35, 1.65), (p<0.001 compared with paroxysmal)
Disertori 2013 [13] Subgroup analysis from a RCT (*1 year follow-up)*	Paroxysmal AF: n/N=771/1442 (53.5%)	AF was defined as paroxysmal if the AF was self-terminating, usually within 48 hours, although AF could continue for up to 7 days; AF was defined as persistent when the AF episodes lasted longer than 7 days. Arrhythmia termination by cardioversion did not change the classification of AF.	Mean age: 66.8 (SD 9.8) years % male: 55%	**Death** 9 (1.2%)
	Persistent AF: n/N=463/1442 (32.1%) *Categorisation was not made in the remaining 14.4% of patients*		Mean age: 68.8 (SD 8.5) years, p=0.0002 % male: 71%, p<0.0001	**Death** 3 (0.65%) Adjusted HR 0.52 (95% CI: 0.13, 1.03), p=0.35
Lip 2014 (*1 year follow-up*); Proietti 2017 [18] *(2 year follow-up)*	Paroxysmal AF: n/N=693/2589 (26.8%)	Not reported	Mean age: 66.7 years (SD 11.4) % male: 58%	**Ischaemic/haemorrhagic stroke death** 1 year: 2/808 2 years: - (*denominators are not clear – we have extracted data on*

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke mortality
Prospective cohort *(up to 2 years follow-up)*				*what appears to be all participants enrolled within each group*)
	Persistent AF: n/N=550/2589 (21.2%)		Mean age: 67.9 years (SD 11.0) % male: 60%	**Ischaemic/haemorrhagic stroke death** 1 year: 1/647 2 years: 1/430
	Long-standing persistent AF: n/N=121/2589 (4.7%)		Mean age: 70.9 years (SD 10.8) % male: 61%	**Ischaemic/haemorrhagic stroke death** 1 year: 4/145 2 years: -
	Permanent AF: n/N=451/ 2589 (17.4%)		Mean age: 73.0 years (SD 10.2) % male: 58%	**Ischaemic/haemorrhagic stroke death** 1 year: 1/526 2 years: -
Steinberg 2015 [19] Subgroup *post hoc* analysis from RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2514/14 062 (17.9%)	Patients experiencing episodic AF, self-terminating within 7 days, are said to have paroxysmal AF; patients whose arrhythmia persists beyond 7 days (or requires intervention to terminate) are considered to have persistent AF.	Median age: 72 (25^{th}, 75^{th} percentile: 65, 78) years % male: 55%	**All-cause mortality** Events/100 patient years (total events): 3.52 (170)
	Persistent AF: n/N=11548/14 062 (82.1%)		Median age: 73 (25^{th}, 75^{th} percentile: 65, 78) years, p=0.033 % male 61%, p<0.001	**All-cause mortality** 4.78 (1029) Adjusted HR: 0.79 (95% CI 0.67, 0.94), p=0.0061

AF: Atrial fibrillation; CI: Confidence interval; ECG: Electrocardiogram; HR: Hazard ratio; IQ: Interquartile range; NA: Not applicable; NIHSS: National Institutes of Health Stroke Scale; NR: Not reported; NVAF: Non-valvular atrial fibrillation; SD: Standard deviation; TE: Thromboembolism

Question 1b: Asymptomatic vs. symptomatic AF

Two studies presented comparative data for patients with asymptomatic versus symptomatic AF (Potpara 2013; Rienstra 2014) [21, 22]. Potpara (2013) [21]was a prospective cohort study with baseline and 10 year follow-up data, and Rienstra (2014) [22] presented a subgroup analysis of data from a RCT, with baseline and mortality data collected at 2.3 (± 0.6) years follow-up.

One study reported that patients with asymptomatic AF were significantly younger (67 vs. 69 years, p=0.0111) (Rienstra 2014) [22], while the other study did not find a statistically significant difference in age between the patient groups (p=0.61) (Potpara 2013) [21]. The mean age of the patients in the study by Potpara (2013) [21] was 53.1 (SD 13.1) years and 52.6 (SD 12.1). In both studies, higher percentages of males were asymptomatic than symptomatic (p values were <0.001 Potpara 2013 [21] and 0.007 in Rienstra 2014 [22]); the opposite was true for females. Details of these studies are summarised below and in Appendix 3, Table 3.3 and 3.4.

Evidence from one study demonstrated significantly more ischaemic stroke events in patients with asymptomatic AF compared to patients with symptomatic AF, but not for other types of stroke. Results for stroke risk were inconsistent between the two studies that reported this information. Both studies reported on cardiovascular death, and both found no significant differences between patients with asymptomatic AF and symptomatic AF.

The detailed results are described below and in Table 8.

Stroke

Only one study, the prospective cohort with 10 year follow-up data (Potpara 2013) [21], reported on stroke. Stroke or systemic thromboembolic events did not significantly differ between patients with asymptomatic or symptomatic AF (HR: 1.6 [95% CI: 1.0, 2.8], p=0.08), but there were significantly more ischaemic stroke events in patients with asymptomatic AF compared to patients with symptomatic AF (HR: 2.1 [95% CI: 1.2, 3.9], p=0.02).

Stroke risk

Both studies reported on stroke risk factors. Rienstra (2014) [22] reported mean CHADS2 scores, which were significantly higher in patients with

[11] Data and significance value as reported by study authors, although values in groups appear similar.

symptomatic AF (1.7 [SD 1.1] vs. asymptomatic AF patients (1.2 [SD 1.1], p<0.001). Potpara (2013) [21] reported the percentage of patients with different CHADS2 and CHA2DS2VASc scores (0, 1 and ≥2). For the higher score categories, there were no significant differences between patient groups, but the authors reported that asymptomatic AF patients had a higher prevalence of CHA2DS2VASc score of 0 (p=0.02).

Stroke mortality

Two studies reported on cardiovascular death (Potpara 2013; Rienstra 2014) [21, 22]. Cardiovascular death, and all-cause mortality did not differ significantly between patients with asymptomatic and symptomatic AF (Adjusted12 HR: 0.9 [95% CI: 0.4, 1.9], p=0.832 and Adjusted HR: 0.8 [95% CI: 0.4, 1.6], p=0.612, respectively) in Potpara (2013) [21]. Similarly, death from cardiovascular causes did not significantly differ between patient groups (Absolute difference: -2.6 [95% CI: -7.1, 2.0], p=0.27).

Table 8. Studies relevant to criterion 1 (question 1b): stroke, stroke risk and stroke mortality

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
Potpara 2013 [21] Prospective cohort (**baseline data and 10 years follow-up**)	Asymptomatic AF: n/N = 146/1100 (13.3%)	Asymptomatic AF was defined as AF documented by 12-lead ECG during regular visit, in the absence of any new symptoms (e.g. palpitations, tachycardia, fatigue, malaise, etc.) or worsening of pre-existent symptoms related to other illness. In patients without pre-existent medical conditions, AF was diagnosed accidentally during medical examination for other reasons (for example, annual	Mean age: 53.1 (± 13.1) years % male: 83.6%	Any stroke or systemic thromboembolic event: 17 (11.6%) Ischaemic stroke: 14 (9.6%)	% $CHADS_2$ score 1: 56 (38.4%) % $CHADS_2$ score ≥2: 21 (14.4%) % CHA_2DS_2-VAS_C score 1: 42 (28.8%) % CHA_2DS_2-VAS_C score ≥2: 48 (32.9%)	**Cardiovascular death** 8 (5.6%) **All cause death** 10 (6.8%)
	Symptomatic AF: n/N = 954/1100 (86.7%)		Mean age: 52.6 (± 12.1) years, p=0.61 % male: 61.7%, p<0.001	Any stroke or systemic thromboembolic event: 71 (7.4%) HR 1.6 (95% CI 1.0, 2.8), p=0.08	% $CHADS_2$ score 1: 418 (43.8%), p=0.22 % $CHADS_2$ score ≥2: 96 (10.1%), p=0.12	**Cardiovascular death** 54 (5.8%) HR 0.9 (95% CI 0.4, 1.9), p=0.83 **All cause death**

[12] Adjusted for age, gender and treatment at baseline and throughout the follow-up.

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
		examinations of employees, medical examination for driver's licence), and was labelled as first-diagnosed asymptomatic AF only if there was an evidence of sinus rhythm in the previous 12 months and the patient denied any recent change in the self-perception of his/her physical condition.		Ischaemic stroke: 44 (4.6%) HR 2.1 (95% CI 1.2, 3.9), p=0.02	% CHA_2DS_2-VAS_C score 1: 333 (34.9%), p=0.15 % CHA_2DS_2-VAS_C score ≥2: 348 (36.5%), p=0.40	75 (7.9%) HR 0.8 (95% CI 0.4, 1.6), p=0.61
Rienstra 2014 [22] Subgroup data from a RCT **(mean follow-up 2.3 ± 0.6 years)**	Asymptomatic AF: n/N = 157/522 (30%)	Not reported	Mean age: 67 (± 9) years % male: 72%	NR	Mean $CHADS_2$ score: 1.2 (SD 1.1)	**Death from cardiovascular causes** 8 (5%)
	Symptomatic AF: n/N = 365/522 (70%)		Mean age: 69 (± 9) years, p=0.01 % male: 60%, p=0.007		Mean $CHADS_2$ score: 1.7 (SD 1.1), p<0.001	**Death from cardiovascular causes** 28 (8%) Absolute difference -2.6 (95% CI: -7.1, 2.0), p=0.27

AF: Atrial fibrillation; ECG: Electrocardiogram; NR: Not reported; SD: Standard deviation

Risk of bias

Of the two studies that compared asymptomatic AF with symptomatic AF, one was a post hoc analysis following a RCT (Rienstra 2014) [22] and very few details of the trial methodology were reported, so that it had an unclear risk of bias. However, results from this subgroup data should be considered as exploratory. Potpara (2013) [21] was a cohort study and was well conducted for this type of study.

A detailed critical appraisal for each included publication is presented in Appendix 3, Tables 3.19 and 3.20.

Summary of Findings Relevant to Question 1 Criterion 1: Criterion uncertain

Paroxysmal AF vs. persistent or permanent AF

There is consistent evidence that the number of stroke events are significantly higher in patients with permanent AF compared with paroxysmal AF, but differences in the number of stroke events between persistent AF and paroxysmal AF are less consistent. There is also consistent evidence that stroke risk, measured using mean $CHADS_2$ and CHA_2DS_2-VASc scores, or percentage of patients with $CHADS_2$ and CHA_2DS_2-VASc scores ≥2 (indicating high risk of stroke), is significantly higher in patients with permanent AF compared with patients with paroxysmal AF. Similarly to the number of stroke events, the magnitude of difference in stroke risk between persistent AF and paroxysmal AF is less consistent. Only one study investigated ischaemic/haemorrhagic stroke deaths, but the data were not clearly reported and no statistical comparisons were reported in this study for the groups of interest to this rapid review.

Asymptomatic vs. symptomatic AF

Results from one study demonstrated significantly more ischaemic stroke events in patients with asymptomatic AF compared to patients with symptomatic AF, but not for other types of stroke. Results for stroke risk were inconsistent between the two studies that reported this data. Two studies reported on cardiovascular death, and both reported no significant differences between patients with asymptomatic AF and symptomatic AF.

Although there are some clear patterns in the data, we cannot be certain about the study results. This is because the studies did not always use the same methods to analyse the data, and because baseline factors other than type of AF (not explored as part of this rapid review) may have had an independent impact on stroke or stroke mortality. As several data were derived from subgroup analyses, results from these analyses should be considered as exploratory only.

Question 2 Criterion 9

There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered.

Question 2a – What is the benefit of treating screen-detected AF?

Question 2b – Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?

Eligibility for inclusion in the review question

The eligibility criteria according to population, intervention, comparator, outcome and study design (PICOS) are as follows:

Population

For question 2a, eligible studies had to assess:

- adults >65 years of age with screen detected AF who received treatment compared to
- adults >65 years of age with screen detected AF who did not receive treatment

For question 2b, eligible studies had to assess:

- formal screening programmes for AF in adults >65 years (any type of screening strategy) followed by treatment compared to
- routine clinical diagnosis of AF in adults >65 years (presentation with symptoms) followed by treatment

Intervention and Comparator

For question 2a, eligible studies had to compare anticoagulation treatment for the prevention of stroke versus no anticoagulation treatment. A comparator was not relevant for question 2b. For both questions, eligible anticoagulant treatments included:

- apixaban
- dabigatran etexilate
- edoxaban
- rivaroxaban

- vitamin K-antagonists (warfarin, acenocoumarol and phenindione only)
- heparin (heparin, dalteparin sodium, enoxaparin sodium, and tinzaparin sodium only)

Outcomes

Eligible studies had to evaluate one or more of the following outcomes:

- stroke
- stroke risk
- stroke mortality
- all-cause mortality
- thromboembolic events
- congestive heart failure
- cognitive dysfunction
- QoL
- improvement of symptoms/episodes of AF
- adverse effects (AE)/Unintended consequences of oral anticoagulants

When reported in any of included studies, we also planned to stratify the outcomes by patient age.

Study types

The following study designs were prioritised: systematic reviews of RCTs, case control, and comparative cohort studies. We also attempted to find relevant case control studies, and comparative cohort studies, but none were identified.

Limits

Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, none of which addressed question 2a or question 2b.

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

Question 2a: What is the benefit of treating screen-detected AF?

No studies were identified that compared outcomes in adults >65 years of age with screen detected AF who received treatment compared with those who did not receive treatment.

Question 2b: Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?

No systematic reviews studies (RCTs, case control, and comparative cohort studies), or individual case control, and comparative cohort studies (published from 2011 onwards), were identified that compared formal screening programmes for AF in adults >65 years with routine clinical diagnosis of AF (*however, see question 4 which is the same question but only includes RCT evidence*). Initially, one systematic review appeared relevant to this question (Lowres (2013)) [58], but it was deemed ineligible because it included adults younger than 65 years as well as adults 65 years and older, and it did not fully report relevant results (i.e. stroke risk data were not presented for all of the studies that apparently reported it).

Summary of Findings Relevant to Question 2 Criterion 9: Criterion not met

This criterion was not met as no relevant systematic reviews or primary studies were identified that met the inclusion criteria for the review questions related to this criterion.

Question 3 Criterion 4

There should be a simple, safe, precise and validated screening test.

Question 3 – What is the reported accuracy of screening tests for all types of AF?

Eligibility for inclusion in the review

Population

For this question, eligible studies had to assess adults >65 years of age.

Screening Test and Tester

Studies were eligible for inclusion if they investigated the accuracy of a single screening test for AF or a combination of screening tests, recording which health professional conducts the screening test.

Reference Test and Tester

Studies were eligible for inclusion if they compared the index test to the reference test (12-lead ECG performed and read by a cardiologist).

Outcomes

Measures of diagnostic accuracy of the screening test included:

- sensitivity
- specificity
- positive predictive value (PPV)/Negative predictive value (NPV)

When possible, we planned to conduct sub-group analyses by the type of healthcare professional who interpreted the test. We also planned to stratify the outcomes by patient age and type of AF detected.

Study types

We prioritised systematic reviews of diagnostic test accuracy studies.

In addition, we included individual diagnostic test accuracy (DTA) studies (consecutively enrolled populations) that post-dated any relevant systematic reviews.

Limits

Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, of which one systematic review (a health technology assessment [HTA]) and three studies were judged to be relevant to this criterion/question.

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

One systematic review (a HTA) (Welton 2017) [26] and three recently published diagnostic accuracy studies (Hald 2017; Kristensen 2016; Svennberg 2017) [23-25] addressed this research question. Details of these studies are summarised narratively below and in Appendix 3, Tables 3.5 to 3.8.

The HTA (published in 2017 with search dates to December 2015) aimed to determine the diagnostic accuracy of screening tests for detecting AF in adults who have not sought medical attention in a primary or community care setting on account of symptoms associated with AF, and to determine the diagnostic accuracy of screening tests in systematic opportunistic, targeted and population screening settings. The index test could be any non-invasive test for AF that could be utilised in a primary care setting or in the community. The reference standard was a 12-lead electrocardiogram (ECG) interpreted by a cardiologist. Fifteen studies of screening tests for the detection of AF, including a 12-lead ECG, single-lead ECGs, between 1- and 12-lead ECGs, pulse palpation, modified blood pressure monitors, photoplethysmography and two-stage testing were identified.

In this HTA, ten studies were single gate studies, three were two-gate studies and two studies had designs that were unclear. Four of the fifteen studies were conducted in primary care, the other studies were conducted in outpatient settings, secondary or tertiary care settings, or a mixture of outpatient and secondary care or tertiary care settings. In one study the setting was unclear.. Age was an inclusion criterion in seven studies. Participants had to be ≥ 18 years in two studies, ≥ 35 years in one study, ≥ 60 years in one study, ≥ 65 years in two studies and ≥ 75 years in one study.

The majority of patients in the included studies were aged between 65 and 75 years. Seven of the studies excluded patients with a pacemaker and/or an implanted defibrillator (in some cases only if they were in active pacing mode). Only seven studies reported any characteristics of the included cohorts and, of these, only three reported on comorbidities and/or treatments received. Study and participant characteristics are not reported for individual included studies, in this report.

Of the three individual test accuracy studies published after the HTA was completed, one investigated the prevalence of undiagnosed AF patients among consecutively screened patients in routine daily clinical practice in Denmark between January and March 2016 (Hald 2017) [23]. Consecutive patients visiting one of 49 GP clinics in Denmark were asked to participate and included a total of 970 patients. The patients entered in the opportunistic screening study and the individual primary care practices were cluster randomised to one of the three age groups: 65–74 years, 75–84 years, and ≥85 years, respectively. The authors compared pulse palpation conducted by a clinic nurse with 12-lead ECG with interpretation by specialists conducted for all patients who had an irregular pulse.

Kristensen (2016) [24] aimed to evaluate how well an inexpensive portable three-lead ECG monitor PEM identified patients with atrial fibrillation compared to a normal 12-lead ECG between April 2014 to February 2015. The authors invited two groups of patients from one GP clinic in Denmark. One group consisted of patients with known paroxysmal AF and the second group consisted of patients who came for an annual routine health check. The authors aimed to include 30–50% with a diagnosis of AF and 50–70% without AF. A 30 second three-lead recording using a PEM device (Portable ECG Monitor, Beijing Choice Electronic Technology Co., Ltd., Beijing, China) was conducted and the ECG data were transferred from the PEM to a personal computer and were evaluated after printing. The comparator, a 12-lead ECG interpreted by a senior GP or cardiologist, was also conducted.

The STROKESTOP study (Svennberg 2017) [25] aimed to validate the performance of an AF screening algorithm compared with manual ECG analysis. All individuals born in 1936 or 1937 and living in Stockholm county (n = 23 888) or in the rural region of Halland (n = 4880) at the end of 2011 were randomised in a 1:1 fashion to be invited by mail to participate in a screening programme, or to enter a control group. Handheld one-lead device (www.zenicor.com) for intermittent ECG recordings were used by participants during a 2-week period. Participants were instructed to register ECGs using their thumbs two times a day. The device had an integrated mobile transmitter that sends 30 s ECG strip data to a database. These results were compared to the same hand held one-lead device where ECG recordings

were manually interpreted by specially trained research nurses, and all abnormal ECGs were referred to the investigating cardiologist. When results were unclear, referral for interpretation by a consensus group was used.

Across all primary studies [23-25] there were similar numbers of male and female patients. The Hald and STROKESTOP trials [23, 25] included older patients with mean ages over 75 years while the Kristensen (2016) trial [24] included a large age range (18 years to 92 years) with a mean age of 67. Between half and one third of patients had hypertension across the three studies and fewer people had other co-morbid conditions. In the STROKESTOP study [25], participant characteristics were reported in a previous publication [59] and included participants with known AF (n=666), patients with new AF diagnosed during the study (n=218) and patients with no AF (n=6289).

Overall, the recent systematic review (HTA) suggested that pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings would be appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear. Additional diagnostic studies published after this systematic review support this conclusion.

The detailed results are described below.

Sensitivity and specificity, and positive predictive value (PPV)/ Negative predictive value (NPV)

The summary of findings from the systematic review were as follows (with detail in Table 9):

"This review of 15 studies of screening tests for detecting AF found that most tests had a sensitivity (probability of detecting AF in patients with AF) in excess of 0.9. In support of the view that screening could be carried out in primary care, 12-lead ECG interpreted by a GP had a sensitivity of 1 (95% CrI 1 to 1) and also a high specificity of 0.97 (95% CrI 0.84 to 1). Photoplethysmography also had a sensitivity of 1 (95% CrI 1 to 1), but with a lower specificity of 0.87 (95% CrI 0.52 to 0.99). Specificity was in general lower than sensitivity for all of the tests and was lowest for pulse palpation by a nurse (specificity 0.79), 12-lead ECG interpreted by a nurse (specificity 0.84) and photoplethysmography (specificity 0.87). Tests with the highest DOR were the 12-lead ECG (regardless of interpreter), between 1- and 12-lead ECG (automatic or cardiologist interpretation), two-stage tests and

single-lead ECG interpreted by a GP, with all of these tests having similar DORs.

Table 9. Results from the Welton (2017) review

Screening test	Number of studies	Sensitivity (Credible intervals)	Specificity (Credible intervals)	Diagnostic Odds Ratio (Credible intervals)
Modified blood pressure monitor	2	0.955 (0.864 to 0.992)	0.919 (0.777 to 0.982)	2.51 (2.17 to 2.67)
Single lead ECG	5	0.961 (0.917 to 0.986)	0.94 (0.882 to 0.976)	2.56 (2.42 to 2.65)
Single lead ECG – Automatic/algorithm	3	0.967 (0.9 to 0.995)	0.9 (0.742 to 0.975)	2.46 (2.1 to 2.65)
Single lead ECG - nurse	1	0.929 (0.711 to 0.995)	0.92 (0.7 to 0.992)	2.52 (2.01 to 2.7)
Single lead ECG – GP	1	0.94 (0.671 to 0.999)	0.973 (0.838 to 1)	2.65 (2.31 to 2.72)
Single lead ECG – cardiologist	2	0.959 (0.878 to 0.992)	0.927 (0.802 to 0.984)	2.53 (2.23 to 2.67)
Two stage screening strategy	2	0.943 (0.838 to 0.988)	0.966 (0.9 to 0.992)	2.63 (2.46 to 2.7)
Photoplethysmography	1	1 (1 to 1)	0.867 (0.534 to 0.987)	2.39 (1.71 to 2.68)
12-lead ECG	7	0.927 (0.859 to 0.968)	0.974 (0.95 to 0.989)	2.65 (2.59 to 2.69)
12-lead ECG – Automatic/algorithm	6	0.903 (0.803 to 0.961)	0.98 (0.958 to 0.993)	2.67 (2.61 to 2.7)
12-lead ECG – nurse	1	0.967 (0.824 to 1)	0.84 (0.484 to 0.982)	2.33 (1.62 to 2.67)
12-lead ECG – GP	1	1 (1 to 1)	0.973 (0.843 to 1)	2.65 (2.32 to 2.72)
>1 and <12 lead ECG	2	0.839 (0.553 to 0.973)	0.993 (0.978 to 0.999)	2.7 (2.66 to 2.72)
>1 and <12 lead ECG – Automatic/algorithm	1	0.83 (0.474 to 0.978)	0.985 (0.937 to 0.999)	2.68 (2.55 to 2.71)
<1 and <12 lead ECG – cardiologist	1	0.981 (0.756 to 1)	1 (0.999 to 1)	2.72 (2.72 to 2.72)
Pulse palpation	2	0.916 (0.75 to 0.986)	0.788 (0.51 to 0.945)	2.21 (1.67 to 2.57)

Crl: credible interval, ECG: electrocardiogram, N: number of trials, n: number of participants

Hald (2017) [23] reported that eighty-seven of the total 970 patients included in the study (9%) were detected with an irregular pulse, representing 4.4% of patients aged 65-74 years, 10.5% of patients aged 75-84 years and 22.9% of patients aged 85 or older. Assessment of ECG by the GP showed suspicion of AF in 13 patients with final verification of electrocardiograms by cardiologists revealing 10 AF-patients. The highest detection rate of AF was found in the >85 age group (3.39%) followed by the 65-74 age group (0.83%)

and the 75-84 age group (0.54%). Although this study reported PPVs, no false negative were reported so it is not possible to verify the accuracy of the PPVs. Details in Table 10.

In the study by Kristensen (2016) [24] the sensitivity of diagnosing AF by PEM recordings was 86.7% and the specificity was 98.7% when compared to a 12-lead ECG. According to the cardiologist, the misclassification of three PEM recordings were due to interpretation errors and not related to the PEM recording per se. With a high PPV (92.86%) and a high NPV (97.33%) the authors concluded that the PEM device is well suited to detect AF in general practice population. Details in Table 10.

In the study by Svennberg (2017) [25] a computerised algorithm was used to analyse 80,149 ECG recordings in 3,209 individuals. The computerised 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 algorithm interpretation reported a good sensitivity of 97.84%, that is, the algorithm was good at ruling out AF in people who did not have an irregular rhythm and a lower specificity of 88.2%, that is, the algorithms ability to rule in AF when a patient did have an irregular rhythm. Details in Table 10.

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%). With the high sensitivity, the authors concluded that automatic ECG screening using a computerised algorithm safely identifies normal ECGs in and reduces the need for manual evaluation of individual ECGs with >85% with 100% sensitivity on an individual basis.

Table 10. Results from the Hald (2017), Kristensen (2016) and Svennberg (2017) studies

Trial reference	Screening test	n	Detection rate	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Positive Likelihood Ratio	Negative Likelihood Ratio	Accuracy
Hald (2017) [23]	Pulse palpation interpreted by cardiologist – Total population (>65)	970	1.03% (0.40, 1.67)	NR	NR	11.49%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by cardiologist – 65-74 years	480	0.83% (0.02, 1.65)	NR	NR	19.05%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by cardiologist – 75-84 years	372	0.54% (0.00, 1.28)	NR	NR	5.13%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by cardiologist - >85 years	118	3.39% (0.12, 6.66)	NR	NR	14.81%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by a GP – Total population (>65 years)	970	1.34% (0.62, 2.06)	NR	NR	14.94%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by a GP – 65-74 years	480	1.04% (0.13, 1.95)	NR	NR	23.81%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by a GP – 75-84 years	372	1.08% (0.03, 2.12)	NR	NR	10.26%	NR	NR	NR	NR
Hald (2017) [23]	Pulse palpation interpreted by a GP – >85 years	118	3.39% (0.12, 6.66)	NR	NR	14.81%	NR	NR	NR	NR
Kristensen (2016) [24]	PEM	89	NR	86.67%	98.65%	92.86%	97.33%	64.13	0.14	96.63%

Svennberg (2017) [25]	12 lead ECG interpreted by algorithm	7173	NR	97.84%	88.20%	2.84%	99.99%	9.33	0.02	89.54%

NR: Not reported, N: Number of participants, PEM: portable three-lead ECG monitor

Risk of bias

The systematic review (HTA) was assessed using AMSTAR 2, although we note that this revised tool may not be entirely applicable to diagnostic test reviews (Shea 2017) [60]. Our confidence in the results of this review were rated as high. Risk of bias of the individual studies included in the review itself were assessed by the authors using the QUADAS-2 tool. The HTA authors reported that:

- *four studies were judged to be at low risk of bias for patient selection. Three of the cohort studies reported that consecutive or randomly selected individuals were included and, although no details were provided about the method of inclusion, it seemed possible that it was consecutive in one other study. The three studies with two sets of inclusion criteria (case–control or two-gate studies) and the two studies of unclear study design were judged to be at high risk of bias. The other studies were judged to be at an unclear risk of bias because of concerns over or lack of information on the method of enrolment and/or concerns over or lack of information on exclusion criteria*
- *the majority of the studies were scored as being at low risk of bias on the index test domain*
- *no studies were judged to be at high risk of bias for the reference standard*
- *all studies were judged to be at low risk of bias for the domain of flow and timing*
- *only those studies performed in primary care were judged to have a low level of concern with regard to applicability*
- *studies in which the index test was interpreted by a cardiologist were judged to be less applicable (high level of concern regarding applicability) than studies interpreted in primary care/by an algorithm*
- *all of the studies were judged to have a low level of concern regarding applicability apart from one, because the index test was interpreted by a clinician and validated by a researcher (a cardiac electrophysiologist)*

The quality of the additional three included studies was considered to be good. One cause for concern was the reference standard in the Svennberg (2017) [25] study which was interpretation by a cardiologist of an ECG from a hand held device, whereas the other two studies used conventional 12-lead ECG. Another potential problem was the partial verification bias in the Hald (2017) [23] study. Screening accuracy studies often do not report false negatives because this requires that all patients receive the reference standard, or that patients are followed up over time to the next screening interval. When studies do not report false negatives, it means that we do not

know how many cases of AF were missed. In Hald (2017) [23] only patients who had an irregular pulse on palpation went on to have an ECG.

A detailed critical appraisal for each included publication is presented in Appendix 3, Tables 3.21 and 3.22.

Summary of Findings Relevant to Question 3 Criterion 4: Criterion met

This criterion was met because the evidence is consistent and all studies were considered to have a low risk of bias.

A recent HTA of 15 diagnostic accuracy studies including over 9000 patients suggested that a range of options for screening with reasonable performance values were available. Three additional recently published diagnostic studies in primary care populations that investigated pulse palpation, a portable three-lead ECG monitor and a 12-lead ECG interpreted by an algorithm support this conclusion.

The HTA concluded that pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings would be appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear.

This was based on 2 studies of pulse palpation including 2,664 patients and 2 studies of modified blood pressure monitoring including 1,502 patients. The majority of participants in all four studies were 65 years of age or older. All studies were considered to have a low risk of bias and all four studies were undertaken in primary care which reduces concerns about the applicability of the studies to a general screening population. In terms of reported performance values, the sensitivity and specificity modified blood pressure monitoring was comparable to the other screening options. The specificity of pulse palpation was reported to be lower than the other screening options.

All screening options were non-invasive. However the clinical utility of the tests was not explored in the studies included in the HTA review or in the three additional studies identified by this review.

Question 4 Criterion 11

There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity.

Question 4 – Have randomised controlled trials (RCTs) demonstrated a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?

Eligibility for inclusion in the review

The eligibility criteria according to population, intervention, comparator, outcome and study design (PICOS) are described here.

Population

For this question, eligible studies had to assess adults >65 years of age.

Intervention and comparator

Studies were included that compared formal screening programmes for AF in adults >65 years (any type of screening strategy) versus routine clinical diagnosis of AF (presentation with symptoms).

Where possible, we aimed to report data on the frequency and interval of screening.

Outcomes

We included studies that evaluated one or more of the following outcomes:

- stroke
- stroke risk
- stroke mortality
- all-cause mortality
- cardiovascular events
- thromboembolic events
- congestive heart failure
- cognitive dysfunction
- QoL
- improvement of symptoms/episodes of AF
- incidental outcomes e.g. atrial flutter
- adverse effects
- harms of screening

When reported in any of included studies, we planned to stratify outcomes by patient age.

Study types

For this question, systematic reviews of RCTs were prioritised, followed by RCTs.

Limits

Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, of which two systematic reviews and two additional RCTs were judged to be relevant to this criterion/question.

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

Two systematic reviews, including a HTA (reported in four publications) (Moran 2013; 2015; 2016; Welton 2017) [26, 29, 30, 61] and an additional two recently published RCTs (González Blanco 2017; Halcox (2017) [27, 28] presented data that did not perfectly address this research question, but which may be of interest to the NSC. Details of these studies are summarised narratively below and in Appendix 3, Tables 3.9 to 3.12.

Both the systematic reviews reported results for the SAFE trial, and on an overview, this trial appears to match the inclusion crtieria for the above question. The SAFE RCT compared ‘systematic screening’ (i.e. patients ≥ 65 years received a letter inviting them to attend an ECG screening clinic) and ‘opportunistic screening’ (i.e. records of patients ≥ 65 years were flagged to prompt a GP to check a patients pulse if they attended the practice for any reason). As such, both of these strategies could be considered as a ‘formal’ screening programmes as opposed to ‘routine care’ where patients present with AF symptoms to the GP. Although a control group was included in this study, comparisons between interventions and controls were not reported for the outcomes of interest. One of the systematic reviews (the HTA) also included an apparently relevant RCT which compared a formal screening programme with no screening, but the systematic review authors did not summarise the clinical outcomes assessed by this study (Welton 2017) [26].

We therefore, identified the original RCT (Benito 2015) [62] to obtain this data (see below).

Similarly, one potentially relevant RCT (González Blanco 2017) [27] compared 'active, selective search for patients with symptoms and/or signs suggestive of AF' with 'opportunistic screening' (i.e. patients attending a GP for any reason were screened for AF), so it is not clear if this study evaluates a 'routine care'. In addition, results that may be potentially relevant to this rapid review were 'other electrocardiographic alterations', but very little detail was provided regarding what this outcome entailed.

The second potentially relevant RCT compared a programme where one group of patients were given an AliveCor Kardia monitor attached to an iPod to obtain ECGs with remote interpretation, while other patients were randomised to routine care (Halcox 2017) [28]. It is debatable whether or not this trial evaluates a screening programme *per se*. It was suggested by the authors, however, that this approach could be considered for AF screening in routine practice so we reported this study to be inclusive.

Overall, we found that there was not enough evidence to determine whether there is a benefit of formal screening programmes for AF over and above diagnosis of AF only through routine clinical practice. This is because very few studies actually compared formal screening versus routine clinical diagnosis, and very few studies adequately reported relevant clinical health outcomes.

A brief overview of the studies and their results are as follows:

One systematic review and its subsequent updates (Moran 2013; 2015; 2016) [9, 29, 30] included RCTs that compared one or more screening strategies with no screening (routine practice). The second systematic review (a HTA by Welton 2017) [26], *was also an update of the Moran Cochrane review*, but additionally included studies that compared two or more screening strategies as well as a screening strategy versus a no screening arm. As such, we have considered these two systematic reviews separately.

The Moran systematic review included three trials while the Welton (2017) [26] systematic review included the same three RCTs plus two additional RCTs, for a total of five trials. Given that the primary objective of both these systematic reviews was to investigate whether there was a difference between screening strategies on the detection of new cases of AF, not all studies included in these reviews were relevant to this rapid review. Only two trials (both also identified as relevant in our search strategies) addressed

outcomes of relevance to this NSC systematic review: the SAFE [63] and EARLY [62] trials.

The SAFE trial was reported in both the Moran (2013; 2015; 2016) [9, 29, 30] and Welton (2017) [26] systematic reviews. In this cluster-RCT (involving a two-stage randomisation process), fifty selected general practices in the UK were randomly allocated to 25 intervention practices or 25 control practices. In the intervention practices, adults 65 years or older were randomised to a systematic screening (n=5,000) or opportunistic screening arm (n=5,000). Five thousand patients were also randomised to a control group (usual practice). In the systematic screening arm, patients received a letter inviting them to attend an electrocardiogram (ECG) screening clinic. In the opportunistic arm, a flag was placed in the patients' notes to encourage practice staff to take a pulse recording during routine consultation. If their pulse was found to be irregular, individuals were invited to attend a screening clinic. No screening occurred in the control arm. Three relevant outcomes were considered in this trial: adverse events associated with screening, as well as quality of life and anxiety. For these outcomes, however, only the two intervention groups were compared , so that the comparison of interest to this rapid review (i.e. formal screening vs. routine clinical diagnosis) was not fully evaluated in this trial.

For completeness, we present results of comparisons between the two treatment arms (i.e. systematic vs. opportunistic screening) as was reported by Moran (2016) [9]. They summarised that, at the study completion, 479 participants completed the six-item Spielberger State Anxiety Inventory, and 520 completed the five-item EQ-5D instrument. No significant differences were found between the two intervention arms for anxiety (z = -1.699, P value = 0.089) or quality of life (z = -1.166, P value = 0.244). Moran (2016) [9] also stated that no specific adverse events associated with screening were reported, but it was not defined what these might have been. We also note that, as summarised by both Moran (2013; 2015; 2016) [9, 29, 30] and Welton (2017) [26], both types of screening programmes increased the odds of detecting new cases of AF in patients who did not have known AF at baseline, compared to patients in the control group (systematic population screening OR 1.57, 95% CI 1.09 to 2.26; p = 0.017; systematic opportunistic screening OR 1.59, 95% CI 1.10 to 2.29; p = 0.013).The systematic review authors both considered that the SAFE trial had a low risk of bias, but we note that the above results were derived from a subset of patients and may not be as robust as they would be for the full randomised population.

The EARLY trial was only included in the systematic review by Welton (2017) [26], however, Welton did not present some of the outcomes evaluated in this trial that are of interest to this rapid review. In this trial, 4,000 adults aged 65 years or older from

Spain were randomised to screening involving ECG, physical examination and medical history every six months, whereas those in the control group received no screening. The primary outcome of this trial was the proportion of new cases diagnosed at 6 months. Secondary endpoints were the number of new AF diagnoses and complications related to AF. These latter outcomes were considered to be of interest to this rapid review. Two of 463 patients in the intervention group developed treatment-related complications of cutaneous haematomas and bradycardia associated with amiodarone (Benito 2015) [62]. The authors also reported that seven (1.5%) patients in the intervention group and eight of 465 patients (1.7%) in the control group died during the two-year follow-up period, but it was not explicity reported if this was all cause mortality or AF related mortality. We note that at six months, 8 (1.7%) patients in the intervention group and one (0.2%) in the control group had newly diagnosed AF (p=0.018). After 2 years of follow-up, 11 (2.5%) patients in the intervention group and six (1.3%) in the control group had newly diagnosed AF (p=0.132). The systematic review authors identified serious methodological issues with this trial suggesting a high risk of bias.

In addition to the above systematic reviews, we identified two potentially relevant RCTs. One was a cluster RCT by González Blanco (2017) [27] where 'opportunistic screening' for AF detected by pulse palpation on all patients ≥65 years seen by participating healthcare professionals regardless of the reason for the visit (n=5,465), was compared with 'active searching' for symptomatic patients (n=1,525). The primary outcome of this study was the proportion of new cases of AF detected. Over two years, the authors found that a statistically significant greater proportion of cases were detected in the 'active searching' group compared with the 'opportunistic screening' group (6.8% vs. 1.1%; RR 0.16 [95% CI: 0.11, 0.21]). The study authors also reported a significantly higher percentage of other electrocardiographic alterations in the 'active searching' group (10.0% vs. 2.8%; RR 0.20 [95% CI: 0.16, 0.25]). As suggested above, it is debatable whether or not the results from this study address the research question, except that it briefly considers the benefits of different screening programmes on the incidental outcome of other electrocardiographic alterations

The second RCT (the REHEARSE-AF Study) compared twice-weekly patient monitoring with the AliveCor Kardia device (n=500) with routine clinical care (n=501) in patients ≥65 years of age (and with ≥1 additional stroke risk factor) (Halcox 2017) [28]. The primary outcome of this study was time to diagnosis of AF, and secondary outcomes included adverse events. During the 12 month study period, 19 patients were diagnosed with AF in the intervention group and 5 were diagnosed in the control group (HR 3.9 [95% CI 1.4, 10.4] p=0.007). The authors also reported that there were no statistically significant differences between the groups for adverse events: stroke/TIA/SE (HR 0.61 [95% CI 0.22, 1.69], p=0.34), death (p=0.51), clinically significant bleeds

(p=0.56), DVT/PE (p=0.31), 'other cardiovascular' (p=0.27), 'respiratory' (p=0.20), 'other neurological' (p=0.65), 'orthopaedic/musculoskeletal/fall' (p=0.99), 'gastroenterological' (p=0.99), 'renal/urologic' (p=0.26), and 'other' (p=0.78). The authors concluded that "*Regular twice-weekly iECG screening is highly acceptable to people >65 years of age at increased risk of AF and stroke and results in an almost 4-fold increase in the diagnosis of AF over the course of a year. This impact on AF detection and the lower incidence of ischemic strokes/TIAs resulting from AF or undetermined cause with this monitoring strategy suggest a potential clinical benefit warranting further evaluation in a larger outcome trial*."

Risk of bias

Our confidence in the results from these reviews was rated as high. The cluster RCT by González Blanco (2017) [27] was considered to have a high risk of bias and the RCT by Halcox (2017) [28] was considered to have a low risk of bias. As noted above, however, their applicability to this research question is debatable.

A detailed critical appraisal for each included publication is presented in Appendix 3, Tables 3.23 and 3.24.

Summary of Findings Relevant to Question 4 Criterion 11: Criterion not met

Despite identifying two potentially relevant systematic reviews (which collectively, reported on only two RCTs that were subsequently deemed partly relevant to this rapid review question) and a further two recently published RCTs, it is unclear whether there is a benefit of formal screening programmes for AF over and above diagnosis of AF only through routine clinical practice. This is because the included studies did not compare formal screening to routine clinical diagnosis, or did not report relevant outcomes. An upcoming RCT (the SAFER trial: https://www.safer.phpc.cam.ac.uk/) has been identified and will aim to address whether screening for AF is effective and cost effective in reducing stroke and other key outcomes compared to current practice. The feasibility study for this trial has been registered: http://www.isrctn.com/ISRCTN16939438

Question 5 Criterion 14

The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criteria should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.

Question 5 – Is screening for AF in adults cost-effective?

Eligibility for inclusion in the review

The eligibility criteria according to population, intervention, comparator, outcome and study design (PICOS) are described here.

Population

For this question, eligible studies had to assess adults >65 years of age.

Intervention and comparator

Studies were included that compared formal screening programmes for AF in adults >65 years (any type of screening strategy) versus routine clinical diagnosis of AF (i.e. identification of AF by a health care professional during a routine clinical appointment rather than as part of a formal screening programme).

Outcomes

For this question, eligible studies had to evaluate:

- cost-effectiveness measured using quality adjusted life years (QALYs)

Study types

Eligible designs were:

- systematic reviews of cost-utility analyses
- health technology assessments
- cost-utility analyses
- economic models

When reported in any of included studies, we planned to stratify outcomes by patient age. We also planned to capture data on frequency and interval of screening, and length of screening, if reported in the included studies.

Limits

Only publications dated from January 2011 onwards were included. Studies were limited to Europe, United States, Canada, Australia and New Zealand. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, of which one was judged to be relevant to this criterion/question.

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

One systematic review and cost-effectiveness analysis was identified that met the inclusion criteria for this question (Welton 2017) [26]. Six non-UK studies were also identified and are briefly presented in Table 11 below for reference, but are not further discussed. Details of Welton (2017) [26] are summarised narratively below and in Appendix 3, Table 3.3.

Table 11. Non-UK cost-effectiveness studies (for reference only)

Reference		Country	Study objective	Economic evaluation type	Conclusion
Aronsson [64]	2015	Sweden	To estimate the cost-effectiveness of 2 weeks of intermittent screening for AF in 75/76-year-old individuals.	Cost-utility analysis based on a Markov model	Screening for asymptomatic AF in 75/76-year old individuals is cost-effective in Sweden
Aronsson [65]	2017	Sweden	To suggest an optimal age for initiation of screening for unknown AF and to evaluate if repeated screening will add value.	Cost-utility analysis based on a Markov model	Seven designs were deemed cost-effective depending on how much the payer is prepared to pay to gain QALYs. Repeated screening for AF implied additional health benefits to a reasonable cost compared to one-off screening.
Jacobs [66]	2018	The Netherlands	To estimate the cost-effectiveness of screening for AF in those aged at least 65 years in primary care during seasonal influenza vaccination	Cost-utility analysis based on a Markov model	Screening for AF in primary care with a handheld, single-lead ECG device during seasonal influenza vaccination is very likely to be cost saving for identifying new cases of AF with subsequent introduction of stroke prevention
Lowres [67]	2014	Australia	To determine the feasibility, impact and cost-effectiveness of community pharmacy-based screening, using innovative iPhone ECG technology to identify previously undiagnosed AF in people aged 65 years or more.	Cost-utility analysis based on a cross-sectional study	Screening with iECG in pharmacies with an automated algorithm is both feasible and cost-effective.
Moran 2016 [30]		Ireland	To estimate the cost-effectiveness of an opportunistic AF screening programme in primary care in Ireland and investigate the potential impact of differences in the risk of stroke in screen-detected patients with AF	Cost-utility analysis based on a Markov model	Annual opportunistic screening of men and women aged 65 years and older in primary care was likely to be cost-effective.
Tarride [68]	2017	Canada	To conduct an economic evaluation of the Program for the Identification of 'Actionable' AF in the Pharmacy Setting (PIAAF–Pharmacy).	Cost-utility analysis based on a decision analytical model	Screening people aged 65 years or more for AF in pharmacies was highly cost-effective compared to no screening.

AF: Atrial fibrillation; ECG: Electrocardiogram; QALY: Quality-adjusted life-year

Welton (2017) [26] was a systematic review and cost-effectiveness analysis that compared no screening with systematic opportunistic screening, and systematic population-based screening with postal invites and one reminder in a primary care setting in England and Wales.

The following diagnostic methods were considered in Welton:

- pulse palpation (by nurse)
- modified blood pressure monitor
- photoplethysmography
- ECG
    1. 12-lead.
    2. Single lead.
    3. >1 and ≤12 lead.

For 12-lead ECG, results were interpreted by a GP, a nurse or an algorithm. For single lead ECG, interpretation was also assessed by a cardiologist and for >1 and <12 lead, assessment was only by a cardiologist or by an algorithm. For all screening methods (except for initial 12-lead ECG), a positive initial test was confirmed with 12-lead ECG with interpretation by a cardiologist.

Screening ages from 55 to 80 in 5-year bands were modelled with one off or repeat screening considered. In total, 525 different screening strategies were modelled. Modelling was undertaken probabilistically, with the average values from 10,000 model iterations reported.

The underlying prevalence of AF was taken from a 2013 Swedish study [69] that had been used in a previous report by UK NSC [70]. The estimates of screening strategy effectiveness in identifying people with undiagnosed AF were drawn from the SAFE study which also provided estimates of resource use of screening strategies and diagnostic testing with opportunistic screening [63, 71]. Resource use for diagnostic testing with population screening was assumed. Outcomes for people with AF receiving anticoagulation therapies were drawn from a previously published economic model [72]. All other model parameters were derived from either the SAFE study or studies identified from a non-systematic literature search.

Overall, the results from the model indicated that a national screening programme for AF was likely to represent a cost-effective use of resources. Systematic opportunistic screening was more likely to be cost-effective than systematic population screening.

The model results consistently showed that from the age of 65 years onwards all screening methods and diagnostic strategies would have an incremental cost-effectiveness ratio (ICER) no higher than £10,296 per QALY. As the SAFE study identified more people with AF through opportunistic screening than population screening and as the model assumed that opportunistic screening required less resource, all diagnostic strategies with opportunistic screening were more cost-effective than population-based screening.

For a single screening strategy, the systematic opportunistic photoplethysmography was found to have the highest net monetary benefit for all screening start ages. Net monetary benefit is the monetary benefit of QALYs generated by an intervention minus the costs of the intervention. The authors concluded, however, that the evidence for photoplethysmography is not robust and that there is likely little difference in cost-effectiveness between initial photoplethysmography, pulse palpation or modified blood pressure monitoring.

For a repeat screening strategy, screening every five years from ages 65 years to 80 years inclusive was found to be the most cost-effective repeat screening strategy with an ICER in the region of £7,500 (not reported in the paper but calculated from the cost and QALY results provided).

The authors noted a number of strengths and limitations of the modelling they had undertaken. The strength was essentially the underlying data and the robustness of the existing model for oral anticoagulants from which the majority of the post-screening results were derived.

The weaknesses can be summarised as:

- uptake of screening visits was crudely dichotomised into those under and over 75 years of age
- the repeat screening modelling was not as robust as the single screen model with no modelling of new incident cases
- screening was only undertaken by age and not by other risk factors and there could be differential cost-effectiveness if screening was only for high risk individuals. The authors note that findings from the SAFE study suggest that screening only high risk individuals would be less cost-effective than systematic screening
- gender was not included in the model and the SAFE study had found women less likely to accept confirmatory 12-lead ECG after a positive screening test

- diagnostics were single tests, hence reducing the likelihood of identifying people with AF

The authors concluded that a UK-wide opportunistic screening programme using nurse palpation or modified blood pressure monitors as initial screening methods followed by confirmation diagnosis with 12-lead ECG interpreted by a GP with referral to a specialist for unclear diagnoses is the most cost-effective screening approach. The authors also concluded that screening every 5 years from the age of 65 years to the age of 80 years is also likely to be cost-effective.

The results from this study can be used to draw out four key findings on the cost-effectiveness of AF screening in the UK.

Key finding one: screening for AF, whether opportunistic or population-based, is likely to be cost-effective

The SAFE study provided robust evidence that screening for AF, whether opportunistic or population-based, will identify cases of AF that would go undiagnosed without screening. The costs of screening per patient are low, estimated by Welton to be between £1.54 and £14.26 per patient, whereas economic studies have highlighted the significant economic gain from treating AF. It is therefore unsurprising that Welton (2017) [26] found screening for AF to be cost-effective.

Key finding two: some form of simple initial diagnostic test before confirmation with 12 lead ECG is likely to be more cost-effective than 12-lead ECG testing alone

Initial diagnostic testing using palpation, blood pressure monitors or single lead ECG has lower sensitivity and specificity than using a 12-lead ECG evaluated by a GP. This means that initial testing before 12-lead ECG will miss cases of AF rather than 12-lead ECG is used as the primary screening strategy. However, the Welton model suggests that the number of cases missed will be small with a significant increase in overall screening costs. Whilst a screening strategy that uses initial 12-lead ECG with GP interpretation as the screening technology produces the most QALYs compared to any other screening technology, the ICER for immediate 12-lead ECG over an intial test (such as pulse palpation) before 12-lead ECG is substantially above £20,000 per QALY. Initial testing before confirmation with 12-lead ECG is likely to be the most cost-effective strategy.

Key finding three: repeat screening at five-year intervals appears to be cost-effective compared to no screening, but relative cost-effectiveness compared to single screening has not been determined

No direct comparison was made between single and repeat screening in the Welton study and evidence for repeat screening was not as strong as for single screening. The available evidence would suggest that repeat screening is cost-effective compared to no screening with the most cost-effective strategy likely to be screening every 5 years from the age of 65 years. However, the relative cost-effectiveness of single versus repeat screening has not been determined. The Welton study can therefore be used to justify either single or repeat screening economically, but not to justify the choice of single over repeat screening or vice versa.

Key finding four: The evidence on the relative cost-effectiveness of population-based screening against opportunistic screening is weak

The authors of the Welton (2017) [26] study conclude reasonably strongly that opportunistic screening is more cost-effective than systematic population screening. This result could have been predicted without any modelling taking place as the proportion of people screened was taken from the SAFE study where a higher proportion were screened with opportunistic screening and Welton assumed that the per patient costs of population screening would be significantly higher than opportunistic screening. However, both of these assumptions are questionable.

Firstly, the SAFE study had a far higher rate of people screened opportunistically than had been reported elsewhere, a fact acknowledged by Welton who also pointed out that if rates of opportunistic screening are in line with studies other than SAFE then population screening would be the most cost-effective option. The SAFE study was from 2005 and it may be that ‘alarm fatigue’ is greater in 2018 than in 2005 and flags on patient notes for GPs to undertake activity on patients may now not elicit the same response as was the case in the SAFE study. Additionally, it is reasonable to question whether a GP’s response to a flag in a patient’s notes knowing they are part of a clinical trial may be different to their response in a real world setting – a potential bias that did not exist in the population screening in the SAFE trial.

Secondly, although the resource use for screening attendances for opportunistic attendance was taken from the SAFE trial, for population screening, resource use in terms of nurse and GP time was assumed and was significantly higher than opportunistic screening. The justification for this marked difference was not well made.

There are doubts, therefore, that whereas the available evidence can strongly support screening for AF, whether that screening is opportunistic or population-based cannot be strongly supported. This is further made evident by the fact that in the Welton model every screening strategy considered for each age group was statistically indistinguishable from each other in terms of net monetary benefit with very wide confidence intervals around the central estimate. For example, for opportunistic photoplethysmography at age 65 – the strategy considered most cost-effective by Welton – the net monetary benefit (NMB) was £28,623 with a 95% CI of £9,404 to £52,829. This was not statistically significantly different from the least cost-effective strategy of systematic population screening using >1 and <12 lead ECG which had a NMB of £14,120 with a 95% CI of -£1,270 to £33,500.

Risk of bias

Although only one systematic review examined the cost-effectiveness of screening for AF, this study was considered have a low risk of bias.

A detailed critical appraisal of this publication is presented in Appendix 3, Table 5.25.

Summary of Findings Relevant to Question 5 Criterion 14: Criterion met

One study in a UK setting reported on the cost-effectiveness of screening for AF. This study was considered to have a low risk of bias, and the results can be used to draw out four key findings on the cost-effectiveness of AF screening in the UK:

1. Screening for AF, whether opportunistic or population-based, is likely to be cost-effective;
2. Some form of simple initial diagnostic test before confirmation with 12-lead ECG is likely to be more cost-effective than ECG testing alone;
3. Repeat screening at five-year intervals appears to be cost-effective compared to no screening, but relative cost-effectiveness compared to single screening has not been determined;
4. The evidence of the relative cost-effectiveness of population-based screening against opportunistic screening is weak.

Question 6 Criterion 15

Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme.

Question 6a – Is the current clinical pathway for AF optimised in terms of patient compliance?

Question 6b – Is the current clinical pathway for AF optimised in terms of prescribing patterns for anticoagulants?

Eligibility for inclusion in the review

The eligibility criteria according to population, intervention, comparator, outcome and study design (PICOS) are described here.

Population

For question 6a, eligible studies had to assess adults with AF taking anticoagulants.

For question 6b, eligible studies had to assess prescribers of anticoagulants for patients with AF.

Intervention and comparator

Anticoagulant treatments of interest included:

- apixaban
- dabigatran etexilate
- edoxaban
- rivaroxaban
- vitamin K-antagonists (warfarin, acenocoumarol and phenindione only)
- heparin (heparin, dalteparin sodium, enoxaparin sodium and tinzaparin sodium only)

Outcomes

For question 6a, eligible studies had to evaluate patients' compliance/adherence to anticoagulants.
For question 6b, eligible studies had to evaluate prescribing patterns for anticoagulants.

Study types

For this question, eligible study designs were:

- observational cohort studies
- epidemiological studies
- record linkage studies and audits
- quality and outcomes framework data

Limits

Only publications dated from January 2011 onwards, and studies conducted in the UK, were included. Conference abstracts were excluded.

Description of the evidence

Database searches yielded 10389 results, of which 17 were judged to be relevant to these questions; five addressed question 6a and 14 addressed question 6b (2 of the studies addressed both questions).

Appendix 2 provides the PRISMA diagram showing the study selection process.

Summary of findings

Question 6a: Compliance/adherence to anticoagulants in the UK

Five cohort studies presented data on, or related to, AF patients' compliance/adherence to anticoagulants (Das 2015; Hodgkinson 2011; Johnson 2016; Martinez 2016; Mueller 2017) [31-35]. All of these studies reported data for patients who were *newly prescribed* anticoagulants and derived information from databases such as GRASP, GPRD, or other

similar national administrative databases. With the exception of one study (Hodgkinson 2011) [32], data in the studies are reported from between 2011 and 2014. Details of these studies are summarised narratively below and in Appendix 3, Table 3.14.

It is difficult to compare the data across studies because it is not always clear how the outcomes were measured, and what assumptions the authors had made (e.g. see Johnson 2016) [33]. One of the included studies evaluated adherence using the following method: total days' supply / total days in study) x 100 (Mueller 2017) [35]. In this study, median medication refill adherence was 102.9%[13] (interquartile range 89% to 116%), and 82% of patients had a medication refill adherence greater than 80%.

Overall, the majority of studies reported measures of continuation or persistence with anticoagulants. Some studies aimed to compare data by type of oral anticoagulant (OAC) over time. It is beyond the remit of this rapid review to report more than descriptive data about continuation or persistence rates as reported in the publications. These percentages ranged between 74% and 90% (across studies and treatment types) within 6 months of treatment initiation, and generally appeared to decline over the treatment period (up to 23% in Martinez 2016) [34], with the exception of one study (Johnson 2016) [33].

The detailed results are as follows:

- one study evaluated patients with a diagnosis of AF from UK general practices from 1990 onwards (n=67,857 patients) (Hodgkinson 2011) [32]. The authors reported that the average percentage of time that newly diagnosed AF patients remained on anticoagulants was 61% during the first year, and 27% over a five year period
- the study by Martinez (2016) [34] collected UK data between January 2011 and May 2014 (n=27,514). They reported that medication persistence ranged from 87% to 95% (data were reported separately for novel anticoagulants and vitamin K antagonists) at 90 days, from

[13] This percentage exceeds 100% when the numerator is larger than the denominator. This happens, for example, if patients routinely refill their medications early and have more days' supply than the number of days they are included in a study

77% to 86% at 180 days, from 69% to 82% at 270 days, and from 64% to 79% at 365 days

- the study by Mueller (2017) [35] specifically reported results for discontinuation, persistence, and adherence using data from Scottish patients with AF (n=5,398) collected between September 2011 and June 2014. During the study period, 36% discontinued treatment. Crude persistence rate was 82% at 6 months, 76% at 12 months, and 70% at 18 months. They also reported that median medication refill adherence was 102.9% (interquartile range 89% to 116%), and that 82% of patients had a medication refill adherence greater than 80%
- the study by Johnson (2016) [33] evaluated UK data from December 2012 to October 2014 in 13,089 AF patients. They reported that persistence ranged from 84% to 93% (data were reported by type of treatment) at 3 months' follow up, from 74% to 87% at 6 months' follow-up, and from 74% to 88% at 12 months' follow-up (although the numbers of patients at 12 months follow-up were relatively small)
- one study reported audit data from eight randomly chosen UK practices that appears to have been collected in 2014. They found that after 195 days, 78/87 (90%) of AF patients who had started on a new anticoagulation therapy continued treatment (either on the initial agent or an alternative) (Das 2015) [31]

Risk of bias

All of these studies were well conducted for this type of study. Data derived from the general practice databases were considered to be reliable although it is generally acknowledged that they have certain limitations. For example, the diagnosis of AF may be unverified, and if AF was prescribed in secondary care and unrecorded in the primary care data, it will have been under-represented.

A detailed critical appraisal for each included publication is presented in Appendix 3, Table 3.26.

Question 6b: Prescribing of anticoagulants in the UK

Data on prescribing were taken from 14 publications, including quality and outcomes framework data, and cohort studies (Corteville 2015 [36];Das 2015 [31]; Induruwa 2017 [37]; Isaew 2017 [38]; Gallager 2014 [39]; Kerr 2014 [40]; Lonsdale 2016 [41]; Martinez 2016 [34]; Mazurek 2017 [42]; NHS Blackpool [73]; Quality and Outcomes Framework (QOF) [43-46]). Details of these studies are summarised below and in Appendix 3, Table 3.15.

As above, these results are difficult to compare because the studies variously reported on all AF patients, patients with paroxysmal AF, or persistent/permanent AF, or patients with different risk scores. In addition, some of the data were only reported from newly diagnosed patients, and in other studies, this was not specified. Broadly, the findings in Table 12 show a general increase in prescribing rates from 2000 to 2017.

Risk of bias

Four of the above studies were cohort studies and were well conducted for this type of study (Das 2015 [31]; Isaew 2017 [38]; Martinez 2016 [34]; Mazurek 2017 [42]). Two studies evaluated outcomes after implementation of a screening programme (Induruwa 2017 [37]) or an education and awareness programme (Lonsdale 2016 [41]) but as we only extracted observational data (e.g. baseline characteristics or GRASP-AF data that were also reported), we assessed these studies as if they were cohort studies. Some of the data from Lonsdale (2016) [41] were not clearly reported, so we only included data that were clear, and likely to be reliable. As stated above, information derived from the general practice databases were considered to be reliable although (as noted above) it is generally acknowledged that they have certain limitations.

A detailed critical appraisal for each included publication is presented in Appendix 3, Table 3.27.

Summary of Findings Relevant to Question 6 Criterion 15: Uncertain

Compliance/adherence to anticoagulants in the UK

One cohort study conducted in Scotland reported on medication refill adherence. In this study, 82% of patients had a medication refill adherence greater than 80%. Most studies (which reported data collected between 2011 and 2014) reported measures of continuation or persistence with anticoagulants in patients with AF who were newly prescribed anticoagulants. These percentages ranged between 74% and 90% (across studies and types of oral anticoagulants) up to 6 months following treatment initiation, and generally appeared to decline over the treatment period, but the duration of follow-up is limited.

Prescriptions of anticoagulants in the UK

Data extracted from national databases, reported directly or within studies, broadly show a general increase in prescribing rates from 2000 to 2017. As above, these results are difficult to compare because the studies variously reported on all AF patients, patients with paroxysmal AF, or persistent/permanent AF, or patients with different risk scores.

This criterion is uncertain because, although there is a sufficient volume of evidence on continuation/persistence and on prescribing, we could not directly compare the data, and because further statistical comparisons and evaluations (for example, to determine if compliance is maintained with time, or to determine if prescribing patterns are more or less optimised in patients with different types of AF or stroke risk) would need to be conducted before the above questions may be fully addressed.

Table 12. AF patients prescribed anticoagulants in the UK from 2000 to 2017

Reference	Region (if reported), Data type	2000	2005	2010	2011		2012		2013				2014					2015			2016		2017
		May			Jan	Nov	Jun	Jul	Feb	Mar	Apr	Nov	Mar	Apr	May	Jun	Sept	Mar	Apr	May	Mar	Apr	Mar
Isaew 2017 [38]	UK, Data from THIN	18.8%[14] and 34.2%[15]																		56.2%[16] and 69.4%[17]			
Gallager 2014 [39]	UK, CPRD and HES		11.0%[18]																				
Kerr 2014 [40]}	England, GRASP					53.60%[19]																	
Martinez 2016 [34]	UK, CPRD				41.2%[20]										65.5%[21]								

[14] Paroxysmal AF patients with a $CHADS_2$ ≥1 (n=921). This study aimed to compare trends between paroxysmal versus persistent/permanent AF, so data for patients with all types of AF (together) were not reported. Sample size data calculated from information presented in a table.
[15] Persistent or permanent AF patients with a $CHADS_2$ score ≥1 (denominator=13,014).
[16] Paroxysmal AF patients with a $CHADS_2$ score ≥1 (denominator=7,030).
[17] Persistent or permanent AF patients with a $CHADS_2$ score ≥1 (denominator=46,873).
[18] This study included 16,513 patients with a first diagnosis of AF between 1 January 2005 and 28 February 2010 (newly diagnosed patients). Of these 1816 (11%) were taking anticoagulants. This study was not fully data extracted as this data was briefly reported in a table of participant characteristics, and was not a primary or secondary focus of the study.
[19] Patients with $CHA2DS_2$-VASc score ≥2, 1,016 general practices (denominator=107,949). This study was not fully data extracted as this data was briefly reported in one table, and was not the focus of the study (it was an economic analysis).
[20] Patients (with $CHA2DS_2$-VASc ≥2) who were OAC naïve (n not reported for year; denominator=27,514 overall).
[21] Patients (with $CHA2DS_2$-VASc ≥2) who were OAC naïve (n not reported for year; denominator=27,514 overall).

Reference	Region (if reported), Data type	2000	2005	2010	2011		2012		2013				2014					2015			2016		2017
		May			Jan	Nov	Jun	Jul	Feb	Mar	Apr	Nov	Mar	Apr	May	Jun	Sept	Mar	Apr	May	Mar	Apr	Mar
Das 2015 [31]	UK, GRASP-AF						77 %[22]									95% [23]							
NHS Blackpool [73]	Blackpool, GRASP								55.6 %[24]			59.2 %			60.2 %								
Mazurek 2017 [42]	Darlington, community GP data									47.8 %[25]													
Induruwa 2017 [37]	Cambridge, data from 1 hospital																56%[26] (to Feb 2015)						
Corteville 2015 [36]	West Hampshire, GRASP																56 % [27]	61% [28]					

[22] Patients with AF ('eligible for anticoagulation' (n not reported for year; denominator=5471 overall).
[23] Patients with AF ('eligible for anticoagulation') (n not reported for year; denominator=5471 overall).
[24] Patients with AF (no other information reported).
[25] Patients with AF (mean $CHA2DS_2$-VASc was 3.5 [SD 1.8]) (denominator=2259).
[26] Patients with AF in a secondary setting screened on admission (n=847) (median CHA2DS2-VASc score was 4.4).
[27] Patients with AF at high risk of stroke (CHA2DS2-VASc>1) (n not reported for year; denominator=10,813 overall).
[28] Patients with AF at high risk of stroke (CHA2DS2-VASc>1) (n not reported for year; denominator=10,813 overall).

Reference	Region (if reported), Data type	2000	2005	2010	2011		2012		2013				2014					2015			2016		2017
		May			Jan	Nov	Jun	Jul	Feb	Mar	Apr	Nov	Mar	Apr	May	Jun	Sept	Mar	Apr	May	Mar	Apr	Mar
Quality and Outcomes Framework (QOF) [43-46]	North of England, GPES and CQRS										69.3%[29]			74.5%[30]					78.10[31]			81.46[32]	
	Midlands and East of England										68.1%[33]			73.5%[34]					78.08[35]			81.74[36]	
	London										66.7%[37]			71.2%[38]					74.40[39]			77.85[40]	

[29] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=157,223).
[30] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=153,480).
[31] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=238,735).
[32] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=262,350).
[33] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=165,806).

[34] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=159,377).
[35] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=251,912).
[36] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=271,817).
[37] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=51,110).

[38] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=50,107).
[39] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=74,674).
[40] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=82,020).

Reference	Region (if reported), Data type	2000	2005	2010	2011		2012		2013				2014					2015			2016		2017
		May			Jan	Nov	Jun	Jul	Feb	Mar	Apr	Nov	Mar	Apr	May	Jun	Sept	Mar	Apr	May	Mar	Apr	Mar
	South of England										70.8%[41]			75.9%[42]					78.56[43]			81.31[44]	

[41] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=152,547).

[42] In those patients with atrial fibrillation whose latest record of a CHADS2 score is greater than 1 (denominator=513,017).
[43] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=238,616).
[44] In those patients with atrial fibrillation with a record of a CHA2DS2-VASc score of 2 or more (denominator=261,777).

Review summary

Conclusions and implications for policy

There is some consistent evidence to suggest that stroke events, and stroke risk are significantly greater in patients with permanent AF compared with paroxysmal AF, but differences between persistent AF and paroxysmal AF are less consistent. It is not clear from the literature reviewed, however, if this is a clear causal relationship.

There is a lack of evidence comparing formal screening programmes (including systematic and opportunistic screening programmes) over and above diagnosis of AF through routine clinical practice on clinical health outcomes. There were some studies that compared systematic and opportunistic screening, but they were found to be at high risk of bias. More good quality research in this area is warranted.

There is good quality evidence from a HTA that pulse palpation or modified blood pressure monitors (if available) administered by nurses in primary care settings would be appropriate screening tests, followed by a diagnostic 12-lead ECG interpreted by a trained GP in those who screen positive, with referral to a cardiologist/specialist in cases in which the diagnosis is unclear. Additional diagnostic studies published after this systematic review supported this finding.

One study in a UK setting reported on the cost-effectiveness of screening for AF. This study was considered to have a low risk of bias, and the results can be used to draw out four key findings on the cost-effectiveness of AF screening in the UK:

1. Screening for AF, whether opportunistic or population-based, is likely to be cost-effective.
2. Some form of simple initial diagnostic test before confirmation with 12-lead ECG is likely to be more cost-effective than ECG testing alone.
3. Repeat screening at five-year intervals appears to be cost-effective compared to no screening, but relative cost-effectiveness compared to single screening has not been determined.

4. The evidence of the relative cost-effectiveness of population-based screening against opportunistic screening is weak.

Measures of continuation or persistence with anticoagulants were largely collected between 2011 and 2014 and ranged from between 74% and 90% (across studies and treatment types) within 6 months of treatment initiation, and generally appeared to decline over the treatment period but the duration of follow-up is limited. These data can only be considered as descriptive and further statistical analyses would be needed to fully evaluate trends through time, or trends within a treatment period.

There appears to have been a general increase in prescribing rates of anticoagulants in patients with AF from 2000 to 2017, however, without further statistical analyses, definitive conclusions cannot be made on any trends.

Overall, due to limitations in the amount and quality of literature that address screening and atrial fibrillation, screening is not recommended at this time.

Limitations

There were several limitations of the available evidence. When evaluating studies that compared paroxysmal AF versus persistent AF, one of the study authors reported that rates of stroke differed between different types of AF, but in a multivariate analysis, they found that other baseline factors independently increased adverse events (i.e. including stroke) (Banerjee 2013) [11]. While reporting and evaluating this is beyond the scope of this rapid review, it raises the question regarding the importance of other baseline factors that have a dependent or independent impact on stroke risk alongside type of AF. As such, a question regarding differences in stroke risk by type of AF may not be able to be comprehensively addressed in this rapid review without more complex analyses.

One of the difficulties with the literature is that it was not always reported whether patients received treatment after diagnosis (either through formal screening or clinical diagnosis), and we can only assume that was the case. In addition, some of the adverse outcomes reported in the studies

may be treatment-related. If this is the case, there may be some confounding in *treatment-related* outcomes if fewer patients are detected and treated in one arm compared to another. It is also possible that improved outcomes may be associated with higher detection and subsequent treatment. Thus, it may be important to consider detection rates of different screening strategies alongside any differences in health outcomes observed in these studies.

It was very difficult to compare rates of continuation or persistence with anticoagulants across studies because it was not always clear how the outcomes were measured. We could only describe data as presented by individual studies, but could not draw out any clear patterns over time or within a treatment period.

It was also difficult to compare prescribing rates as the studies variously reported on all AF patients, patients with paroxysmal AF, or persistent/permanent AF, or patients with different risk scores – all of which may have an impact on rates.

Although information derived from the general practice databases were considered to be reliable, it is generally acknowledged that they have certain limitations (e.g. diagnosis of AF may not be verified, and if AF was prescribed in secondary care and unrecorded in the primary care data, it will have been under-represented).

Limitations of the review methodology include a restriction on study countries. This means that some potentially relevant studies may have been missed. As this is a rapid review, the data have not been synthesised using meta-analyses, or other statistical methods. As such, some of the data should be considered as descriptive and may not comprehensively address their associated research questions.

Appendix 1 — Search strategy

The searches are presented for each question.

SEARCH 1: RESEARCH QUESTION 1

Source: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Interface / URL: OvidSP
Database coverage dates: 1946 to Present
Search date: 20/02/18
Retrieved records: 1235
Search strategy:

1 *Atrial Fibrillation/ (36667)
2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kf. (65788)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kf. (42753)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kf. (682)
5 or/1-4 (91332)
6 exp *Stroke/ and (risk/ or risk factors/) (16522)
7 ((stroke or strokes) and (risk or risks)).ti,kf. (8911)
8 ((stroke or strokes) adj6 (risk or risks)).ab. /freq=2 (10660)
9 ((apoplex$ or cva or cvas or cerebrovascular accident$ or vascular accident$ or brain vasc$ or cerebral vasc$) and (risk or risks)).ti,kf. (187)
10 ((apoplex$ or cva or cvas or cerebrovascular accident$ or vascular accident$ or brain vasc$ or cerebral vasc$) adj6 (risk or risks)).ab. /freq=2 (127)
11 (((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$)) and (risk or risks)).ti,kf. (994)
12 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$) adj6 (risk or risks)).ab. /freq=2 (438)
13 ((risk or risks) adj6 (brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$)).ab. /freq=2 (444)

14 (((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)) and (risk or risks)).ti,kf. (907)
15 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$) adj6 (risk or risks)).ab. /freq=2 (463)
16 ((risk or risks) adj6 (brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).ab. /freq=2 (447)
17 or/6-16 (27286)
18 5 and 17 (4851)
19 5 and (exp Stroke/ep or Cerebrovascular Disorders/ep) (2089)
20 18 or 19 (5637)
21 meta-analysis as topic/ (15975)
22 meta-analysis.pt. (84792)
23 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kf. (239437)
24 or/21-23 (262097)
25 20 and 24 (291)
26 case-control studies/ (243134)
27 case-control$.ti,ab,kf. (109578)
28 (Epidemiologic Studies/ or Cohort Studies/ or follow-up studies/ or longitudinal studies/ or prospective studies/ or retrospective studies/ or Cross-Sectional Studies/ or observational study/ or Registries/) and comparative study/ (326652)
29 (Epidemiologic Studies/ or Cohort Studies/ or follow-up studies/ or longitudinal studies/ or prospective studies/ or retrospective studies/ or Cross-Sectional Studies/ or observational study/ or Registries/) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$).ti,ab,kf. (1056452)
30 (epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or

observational or register or registers or registry or registries).ti,ab,kf. and comparative study/ (136721)
31 ((epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$)).ti,ab,kf. (766407)
32 or/26-31 (1659671)
33 20 and 32 (2090)
34 exp Great Britain/ (341134)
35 (national health service* or nhs*).ti,ab,in. (149291)
36 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (88133)
37 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in. (1785618)
38 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. (1164758)

39 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in. (44828)
40 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. (168403)
41 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in. (21079)
42 or/34-41 (2303546)
43 (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp great britain/ or europe/) (2543051)
44 42 not 43 (2181864)
45 exp United States/ (1251323)
46 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,jw,in,kf. (5932646)
47 exp Europe/ or European Union/ (1296447)
48 (europe$ or eu or "eu's" or "e.u." or 5eu or eu5).ti,ab,kf,jw,in. (794271)
49 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kf,jw,in. (5080520)
50 exp Canada/ (142200)
51 (canada$ or canadian$).ti,ab,kf,jw,in. (848023)
52 australasia/ or exp australia/ (126124)
53 (australia$ or australas$).ti,ab,jw,kf,in. (598545)
54 New Zealand/ (35321)
55 new zealand$.ti,ab,jw,kf,in. (152777)
56 or/45-55 (13259001)
57 44 or 56 (14530557)
58 33 and 57 (1628)
59 25 or 58 (1845)
60 exp animals/ not humans/ (4426664)
61 (news or editorial or case reports).pt. or case report.ti. (2552892)
62 59 not (60 or 61) (1841)
63 limit 62 to (english language and yr="2011 -Current") (1239)
64 remove duplicates from 63 (1235)

Source: Embase 1974 to 2018 February 20
Interface / URL: OvidSP

Database coverage dates: 1974 to 2018 February 20
Search date: 21/02/18
Retrieved records: 889
Search strategy:

1 exp *atrial fibrillation/ (15879)
2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kw. (110212)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kw. (72085)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kw. (1466)
5 or/1-4 (141108)
6 exp *cerebrovascular accident/ and (risk/ or risk factor/) (15460)
7 ((stroke or strokes) and (risk or risks)).ti,kw. (15641)
8 ((stroke or strokes) adj6 (risk or risks)).ab. /freq=2 (17347)
9 ((apoplex$ or cva or cvas or cerebrovascular accident$ or vascular accident$ or brain vasc$ or cerebral vasc$) and (risk or risks)).ti,kw. (428)
10 ((apoplex$ or cva or cvas or cerebrovascular accident$ or vascular accident$ or brain vasc$ or cerebral vasc$) adj6 (risk or risks)).ab. /freq=2 (236)
11 (((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$)) and (risk or risks)).ti,kw. (2005)
12 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$) adj6 (risk or risks)).ab. /freq=2 (661)
13 ((risk or risks) adj6 (brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (ischemi$ or ischaemi$ or infarct$ or thrombo$ or emboli$)).ab. /freq=2 (673)
14 (((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)) and (risk or risks)).ti,kw. (1631)
15 ((brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3 (haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$) adj6 (risk or risks)).ab. /freq=2 (658)
16 ((risk or risks) adj6 (brain$ or cerebr$ or cerebell$ or intracerebral or intracran$ or parenchymal or intraventricular or infratentorial or supratentorial or basal gangli$ or vertebrobasilar or hemispher$ or MCA or anterior circulation or posterior circulation) adj3

(haemorrhage$ or hemorrhage$ or haematoma$ or hematoma$ or bleed$)).ab. /freq=2 (641)
17 or/6-16 (39071)
18 5 and 17 (7761)
19 5 and (exp cerebrovascular accident/ep or cerebrovascular disease/ep) (403)
20 18 or 19 (7938)
21 "systematic review"/ or "systematic review (topic)"/ (177397)
22 meta analysis/ or "meta analysis (topic)"/ (171985)
23 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kw. (296184)
24 or/21-23 (392863)
25 20 and 24 (552)
26 exp case control study/ (139546)
27 case-control$.ti,ab,kw. (140346)
28 (Clinical study/ or Family study/ or Longitudinal study/ or Retrospective study/ or Prospective study/ or Cohort analysis/ or observational study/ or register/) and exp comparative study/ (141397)
29 (Clinical study/ or Family study/ or Longitudinal study/ or Retrospective study/ or Prospective study/ or Cohort analysis/ or observational study/ or register/) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$).ti,ab,kw. (948505)
30 (epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries).ti,ab,kw. and exp comparative study/ (102051)
31 ((epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$)).ti,ab,kw. (1173359)
32 or/26-31 (1732499)
33 20 and 32 (2529)
34 United Kingdom/ (387723)

35 (national health service* or nhs*).ti,ab,in,ad. (273504)
36 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (34233)
37 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in,ad. (2839825)
38 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in,ad. (2117368)
39 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in,ad. (85514)
40 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in,ad. (293484)
41 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in,ad. (38501)
42 or/34-41 (3462960)
43 (exp "arctic and antarctic"/ or exp oceanic regions/ or exp western hemisphere/ or exp africa/ or exp asia/ or exp "australia and new zealand"/) not (united kingdom/ or europe/) (2766137)
44 42 not 43 (3285430)

45 exp United States/ (1160934)
46 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,kw,jw,ad. (9250163)
47 exp Europe/ or european union/ (1490295)
48 (europe$ or eu or "eu's" or "e.u." or 5eu or eu5).ti,ab,kw,jw,ad. (1231415)
49 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kw,jw,ad. (7997079)
50 exp Canada/ (163321)
51 (canada$ or canadian$).ti,ab,kw,jw,ad. (980671)
52 exp "Australia and New Zealand"/ (199350)
53 (australia$ or australas$).ti,ab,kw,jw,ad. (709954)
54 new zealand$.ti,ab,kw,jw,ad. (174049)
55 or/45-54 (19513259)
56 44 or 55 (21249258)
57 33 and 56 (2085)
58 25 or 57 (2494)
59 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5801359)
60 editorial.pt. or case report.ti. (812120)
61 conference abstract.pt. (2887402)
62 58 not (59 or 60 or 61) (1363)
63 limit 62 to (english language and yr="2011 -Current") (913)
64 remove duplicates from 63 (889)

Source: Database of Abstracts of Reviews of Effects: Issue 2 of 4, April 2015
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 21/02/18
Retrieved records: 38
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11032
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134

#5 #1 or #2 or #3 or #4 17669
#6 [mh Stroke] and ([mh ^risk] or [mh ^"risk factors"]) 1255
#7 ((stroke or strokes) and (risk or risks)):ti 1045
#8 ((stroke or strokes) near/6 (risk or risks)) 5401
#9 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) and (risk or risks)):ti 5
#10 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) near/6 (risk or risks)) 816
#11 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)) and (risk or risks)):ti 117
#12 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*) near/6 (risk or risks)) 721
#13 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)) 664
#14 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) and (risk or risks)):ti 107
#15 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) near/6 (risk or risks)) 798
#16 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) 802
#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 6983
#18 #5 and #17 1361
#19 5 and ([mh stroke/ep] or [mh ^"Cerebrovascular Disorders"/ep]) 528
#20 #18 or #19 1832
#21 #20 Publication Year from 2011 to 2018 1201
#22 #21 in Other Reviews 38

Source: Health Technology Assessment Database: Issue 4 of 4, October 2016
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 21/02/18
Retrieved records: 6
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11032
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134
#5 #1 or #2 or #3 or #4 17669
#6 [mh Stroke] and ([mh ^risk] or [mh ^"risk factors"]) 1255
#7 ((stroke or strokes) and (risk or risks)):ti 1045
#8 ((stroke or strokes) near/6 (risk or risks)) 5401
#9 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) and (risk or risks)):ti 5
#10 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) near/6 (risk or risks)) 816
#11 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)) and (risk or risks)):ti 117
#12 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*) near/6 (risk or risks)) 721
#13 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)) 664
#14 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) and (risk or risks)):ti 107
#15 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) near/6 (risk or risks)) 798

#16 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) 802
#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 6983
#18 #5 and #17 1361
#19 5 and ([mh stroke/ep] or [mh ^"Cerebrovascular Disorders"/ep]) 528
#20 #18 or #19 1832
#21 #20 Publication Year from 2011 to 2018 1201
#22 #21 in Other Reviews 38
#23 #21 in Technology Assessments 6

Source: Cochrane Database of Systematic Reviews: Issue 2 of 12, February 2018
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 21/02/18
Retrieved records: 19
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)):ti,ab,kw 9805
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib):ti,ab,kw 4611
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib):ti,ab,kw 130
#5 #1 or #2 or #3 or #4 10888
#6 [mh Stroke] and ([mh ^risk] or [mh ^"risk factors"]) 1255
#7 ((stroke or strokes) and (risk or risks)):ti 1045
#8 ((stroke or strokes) near/6 (risk or risks)):ab,kw 4251
#9 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) and (risk or risks)):ti 5
#10 ((apoplex* or cva or cvas or cerebrovascular next accident* or vascular next accident* or brain next vasc* or cerebral next vasc*) near/6 (risk or risks)):ab,kw 781
#11 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)) and (risk or risks)):ti 117
#12 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*) near/6 (risk or risks)):ab,kw 589

#13 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (ischemi* or ischaemi* or infarct* or thrombo* or emboli*)):ab,kw 547
#14 (((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)) and (risk or risks)):ti 107
#15 ((brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) near/6 (risk or risks)):ab,kw 523
#16 ((risk or risks) near/6 (brain* or cerebr* or cerebell* or intracerebral or intracran* or parenchymal or intraventricular or infratentorial or supratentorial or basal next gangli* or vertebrobasilar or hemispher* or MCA or "anterior circulation" or "posterior circulation") near/3 (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)):ab,kw 530
#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 6039
#18 #5 and #17 1103
#19 5 and ([mh stroke/ep] or [mh ^"Cerebrovascular Disorders"/ep]) 528
#20 #18 or #19 1579
#21 #20 Publication Year from 2011 to 2018 1034
#22 #21 in Cochrane Reviews (Reviews and Protocols) 19

SEARCH 2: RESEARCH QUESTIONS 3, 4 AND 5

Source: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Interface / URL: OvidSP
Database coverage dates: 1946 to Present
Search date: 22/02/18
Retrieved records: 792
Search strategy:

1 *Atrial Fibrillation/ (36686)
2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kf. (65884)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kf. (42811)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kf. (681)
5 or/1-4 (91438)
6 *Mass Screening/ (48853)
7 screen$.ti,kf. (163280)
8 (test or tests or tested or testing).ti,kf. (353456)
9 detect$.ti,kf. (328612)
10 or/6-9 (819578)
11 *Pulse/ (5230)
12 (pulse or pulses).ti,kf. (36620)
13 *Photoplethysmography/ (802)
14 (photoplethysmogra$ or photo-plethysmogra$ or photoreflexometr$ or photo-reflexometr$ or light reflection rheogra$ or photoelectric plethysmogra$ or ppg or ppgs).ti,kf. (1394)
15 *Blood Pressure Monitors/ (1313)
16 *Blood Pressure Determination/is [Instrumentation] (1813)
17 ((blood pressure$1 or bp) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kf. (10137)
18 sphygmomanometer$1.ti,kf. (448)
19 *Electrocardiography/ (62438)
20 *Electrocardiography, Ambulatory/ (3285)
21 (electrocardiogram$ or cardiogram$ or electrocardiograph$ or cardiograph$).ti,kf. (39041)
22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs).ti,kf. (13886)
23 holter$ monitor$.ti,kf. (620)
24 *monitoring, ambulatory/ or *blood pressure monitoring, ambulatory/ (8592)
25 ((ambulatory or portable or pocket$1) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kf. (5952)

26 ((outpatient$1 or out-patient$1 or home$1 or remot$) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kf. (7030)
27 (self adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kf. (13852)
28 *Cell Phones/ (5304)
29 (m-health$ or mhealth$ or mobile health$).ti,kf. (3029)
30 ((mobile or smart or cell or cellular) adj3 (phone$1 or telephone$1 or handset$1 or hand-set$1)).ti,kf. (4566)
31 mobiles.ti,kf. (23)
32 ((hand or handheld) adj3 (phone$1 or telephone$1)).ti,kf. (47)
33 smartphone$1.ti,kf. (3162)
34 (iphone$ or i-phone$).ti,kf. (212)
35 *Computers, Handheld/ (2166)
36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) adj3 (comput$ or PC or PCs or system$1)).ti,kf. (1865)
37 (mobile adj3 (communicat$ or technology or technologies or network$1)).ti,kf. (1106)
38 ((mobile or electronic$ or digital$ or device$1 or portable or pocket$1 or handheld or hand-held or palm or palmtop) adj3 tablet$1).ti,kf. (119)
39 (tablet$1 adj3 (comput$ or PC or PCs or device or devices)).ti,kf. (324)
40 (phablet$1 or slate or slates or laplet$1 or mini-tablet$1 or hybrid tablet$1 or convertible tablet$1).ti,kf. (230)
41 (booklet$1 and tablet$1).ti,kf. (0)
42 ((mobile or electronic$ or digital$ or portable or pocket$1 or handheld or hand-held or palm or palmtop) adj3 (device or devices)).ti,kf. (3659)
43 personal digital assistant$1.ti,kf. (323)
44 ((PDA or PDAs) not (ductus arteriosus or posterior descending arter$ or pancreatic ductal adenocarcinoma$)).ti,kf. (1124)
45 (device-based or mobile-based).ti,kf. (513)
46 ((device$1 or mobile) adj2 technolog$).ti,kf. (951)
47 (smart adj (digital$ or device$1 or technolog$)).ti,kf. (124)
48 (ipad$ or i-pad$ or ipod$ or i-pod$).ti,kf. (595)
49 *Mobile Applications/ (2096)
50 (app or apps).ti,kf. (5314)
51 ((mobile or phone$1 or telephone$1 or device$1 or tablet$1 or electronic$ or digital$ or software$1) adj3 application$1).ti,kf. (2705)
52 *Wireless Technology/ or ((wireless or wire-less or wifi or wi-fi or bluetooth$ or blue-tooth$) and (mobile or phone$1 or telephone$1 or tablet$)).ti,kf. (2219)
53 (ubiquitous and (mobile or phone$1 or telephone$1 or device or devices or tablet$1 or wireless or wire-less or wifi or wi-fi or bluetooth$ or blue-tooth$)).ti,kf. (81)
54 smartwatch$.ti,kf. (47)
55 ((mobile or electronic$ or digital$ or digitis$ or digitiz$ or wireless$ or smart) adj3 (patch or patches or monitor$ or watch or watches or wristwatch$ or band or bands or

wristband$ or tracker$1 or cloth$ or garment$ or textile$ or jewellery or bracelet$)).ti,kf. (1988)
56 wearable$1.ti,kf. (3032)
57 (android$ or ios).ti,kf. (381)
58 apple$.ti,kf. (6424)
59 (AliveCor$ or AliveECG$ or Kardia Mobile$ or iTransmit or search-AF or GP-search or iECG$ or ChoiceMMed$ or Beijing Choice$ or MD100E$ or MD-100E$ or MD100-E$ or MD100B$ or MD-100B$ or MD100-B$ or Easy ECG$ or EasyECG$ or Creative Medical$ or Shenzhen Creative$ or Heal Force$ or HealForce$ or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan$ or HCG-801 or HCG801 or dimetek$ or diCare$ or mc1cc or mc1c or m1ca or m1cb or blade micro or mono micro or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics$ or AfibAlert$ or Lohman Tech$ or cardio24$ or mednovis$ or instantcheck$ or readmyheart$ or dailycare biomedical$ or daily care biomedical$ or dc biomed$ or dcbiomed$ or ecgcheck$ or ecg check$ or cardiac designs$ or MyDiagnostick$ or Applied Biomedical Systems$ or Qardio$ or VitalPatch$ or VitalConnect$ or Beat2Phone$ or Beat 2 Phone$ or VitalSygum$ or Vital Sygum$).ti,kf. (32)
60 (contec$ and (pm-10 or pm10 or pm-80 or pm80)).ti,kf. (0)
61 (heartcheck$ or (ecg adj3 pen)).ti,kf. (0)
62 (beurer$ and (ME-80 or ME-90 or ME80 or ME90)).ti,kf. (0)
63 (reka and e100$).ti,kf. (0)
64 ((noninvasiv$ or non-invasiv$) adj4 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kf. (9148)
65 or/11-64 (201437)
66 5 and 10 (2080)
67 5 and 65 (4962)
68 66 or 67 (6559)
69 exp "Sensitivity and Specificity"/ (516977)
70 sensitivity.tw. (685086)
71 specificity.tw. (403633)
72 ((pre-test or pretest) adj probability).tw. (1866)
73 post-test probability.tw. (487)
74 predictive value$.tw. (91691)
75 likelihood ratio$.tw. (12906)
76 or/69-75 (1290312)
77 (diagnos$ adj5 accurac$).ti,ab,kf. (47363)
78 ((posttest or postest) adj probabilit$).ti,ab,kf. (343)
79 (false positive$1 or false negative$1 or true positive$1).ti,ab,kf. (70728)
80 ROC Curve/ or exp Diagnostic Errors/ (151083)
81 roc curve$.ti,ab,kf. (24575)
82 receiver operating characteristic.ti,ab,kf. (43659)

83 observer variation$.ti,ab,kf. (1234)
84 or/77-83 (268588)
85 76 or 84 (1427242)
86 68 and 85 (1607)
87 5 and ((test or tests or tested or testing or screen or detect$) adj5 accura$).ti,ab,kf. (257)
88 86 or 87 (1766)
89 meta-analysis as topic/ (15984)
90 meta-analysis.pt. (84941)
91 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kf. (240058)
92 or/89-91 (262730)
93 68 and 92 (90)
94 Economics/ (26868)
95 exp "Costs and cost analysis"/ (212262)
96 Economics, dental/ (1891)
97 exp "Economics, hospital"/ (22659)
98 Economics, medical/ (8936)
99 Economics, nursing/ (3978)
100 Economics, pharmaceutical/ (2741)
101 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (650244)
102 (expenditure$ not energy).ti,ab. (24949)
103 value for money.ti,ab. (1387)
104 budget$.ti,ab. (25140)
105 or/94-104 (791499)
106 ((energy or oxygen) adj cost).ti,ab. (3613)
107 (metabolic adj cost).ti,ab. (1195)
108 ((energy or oxygen) adj expenditure).ti,ab. (21843)
109 or/106-108 (25758)
110 105 not 109 (785584)
111 Technology Assessment, Biomedical/ (9147)
112 (technology assessment$ or technology appraisal$ or hta or htas).ti,ab,kf. (7247)
113 exp Models, Economic/ (13005)
114 econometric$.ti,ab,kf. (1397)
115 or/111-114 (27517)
116 110 or 115 (796467)

117 68 and 116 (214)
118 randomized controlled trial.pt. (454052)
119 (random$ or placebo).ti,ab,kf. (1032200)
120 or/118-119 (1129380)
121 68 and 120 (474)
122 88 or 117 or 121 (2209)
123 exp Great Britain/ (341258)
124 (national health service* or nhs*).ti,ab,in. (149581)
125 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (88182)
126 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in. (1787459)
127 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. (1166286)
128 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in. (44890)
129 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. (168632)

130 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in. (21108)
131 or/123-130 (2305715)
132 (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp great britain/ or europe/) (2544380)
133 131 not 132 (2183936)
134 exp United States/ (1251855)
135 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,jw,in,kf. (5937679)
136 exp Europe/ or European Union/ (1297081)
137 (europe$ or eu or "eu's" or "e.u." or 5eu or eu5).ti,ab,kf,jw,in. (795122)
138 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kf,jw,in. (5086242)
139 exp Canada/ (142272)
140 (canada$ or canadian$).ti,ab,kf,jw,in. (848875)
141 australasia/ or exp australia/ (126187)
142 (australia$ or australas$).ti,ab,jw,kf,in. (599321)
143 New Zealand/ (35336)
144 new zealand$.ti,ab,jw,kf,in. (152911)
145 or/133-144 (14542604)
146 122 and 145 (1639)
147 93 or 146 (1684)
148 exp animals/ not humans/ (4427654)
149 (news or editorial or case reports).pt. or case report.ti. (2554184)
150 147 not (148 or 149) (1603)
151 limit 150 to (english language and yr="2011 -Current") (801)
152 remove duplicates from 151 (792)

Source: Embase 1974 to 2018 February 21
Interface / URL: OvidSP
Database coverage dates: 1974 to 2018 February 21
Search date: 22/02/18
Retrieved records: 644
Search strategy:

1 exp *atrial fibrillation/ (15895)

2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kw. (110241)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kw. (72104)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kw. (1470)
5 or/1-4 (141142)
6 *screening/ or *mass screening/ or *screening test/ (61827)
7 screen$.ti,kw. (230553)
8 (test or tests or tested or testing).ti,kw. (437372)
9 detect$.ti,kw. (394128)
10 or/6-9 (1019087)
11 *pulse rate/ (4801)
12 (pulse or pulses).ti,kw. (40243)
13 *photoelectric plethysmography/ (1102)
14 (photoplethysmogra$ or photo-plethysmogra$ or photoreflexometr$ or photo-reflexometr$ or light reflection rheogra$ or photoelectric plethysmogra$ or ppg or ppgs).ti,kw. (1940)
15 exp *blood pressure monitor/ (292)
16 ((blood pressure$1 or bp) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kw. (13985)
17 sphygmomanometer$1.ti,kw. (575)
18 *electrocardiography/ or *electrocardiography monitoring/ or *exercise electrocardiography/ or *signal averaged electrocardiography/ (50568)
19 *ambulatory electrocardiography/ or *Holter monitor/ or *holter monitoring/ (1644)
20 *electrocardiogram/ or *electrocardiograph/ (12186)
21 (electrocardiogram$ or cardiogram$ or electrocardiograph$ or cardiograph$).ti,kw. (38361)
22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs).ti,kw. (20750)
23 holter$ monitor$.ti,kw. (1203)
24 *ambulatory monitoring/ or *home monitoring/ or *self monitoring/ or *remote sensing/ or *blood pressure monitoring/ (14696)
25 ((ambulatory or portable or pocket$1) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kw. (9848)
26 ((outpatient$1 or out-patient$1 or home$1 or remot$) adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kw. (9955)
27 (self adj5 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kw. (18865)
28 exp *mobile phone/ (7842)
29 (m-health$ or mhealth$ or mobile health$).ti,kw. (2718)
30 ((mobile or smart or cell or cellular) adj3 (phone$1 or telephone$1 or handset$1 or hand-set$1)).ti,kw. (5729)
31 mobiles.ti,kw. (29)
32 ((hand or handheld) adj3 (phone$1 or telephone$1)).ti,kw. (51)
33 smartphone$1.ti,kw. (3384)

34 (iphone$ or i-phone$).ti,kw. (352)
35 *personal digital assistant/ or *digital computer/ (2007)
36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) adj3 (comput$ or PC or PCs or system$1)).ti,kw. (2344)
37 (mobile adj3 (communicat$ or technology or technologies or network$1)).ti,kw. (1266)
38 ((mobile or electronic$ or digital$ or device$1 or portable or pocket$1 or handheld or hand-held or palm or palmtop) adj3 tablet$1).ti,kw. (159)
39 (tablet$1 adj3 (comput$ or PC or PCs or device or devices)).ti,kw. (394)
40 (phablet$1 or slate or slates or laplet$1 or mini-tablet$1 or hybrid tablet$1 or convertible tablet$1).ti,kw. (280)
41 (booklet$1 and tablet$1).ti,kw. (0)
42 ((mobile or electronic$ or digital$ or portable or pocket$1 or handheld or hand-held or palm or palmtop) adj3 (device or devices)).ti,kw. (4463)
43 personal digital assistant$1.ti,kw. (445)
44 ((PDA or PDAs) not (ductus arteriosus or posterior descending arter$ or pancreatic ductal adenocarcinoma$)).ti,kw. (1899)
45 (device-based or mobile-based).ti,kw. (511)
46 ((device$1 or mobile) adj2 technolog$).ti,kw. (1142)
47 (smart adj (digital$ or device$1 or technolog$)).ti,kw. (142)
48 (ipad$ or i-pad$ or ipod$ or i-pod$).ti,kw. (915)
49 *mobile application/ (2817)
50 (app or apps).ti,kw. (7257)
51 ((mobile or phone$1 or telephone$1 or device$1 or tablet$1 or electronic$ or digital$ or software$1) adj3 application$1).ti,kw. (2954)
52 *wireless communication/ or ((wireless or wire-less or wifi or wi-fi or bluetooth$ or blue-tooth$) and (mobile or phone$1 or telephone$1 or tablet$)).ti,kw. (2062)
53 (ubiquitous and (mobile or phone$1 or telephone$1 or device or devices or tablet$1 or wireless or wire-less or wifi or wi-fi or bluetooth$ or blue-tooth$)).ti,kw. (86)
54 smartwatch$.ti,kw. (38)
55 ((mobile or electronic$ or digital$ or digitis$ or digitiz$ or wireless$ or smart) adj3 (patch or patches or monitor$ or watch or watches or wristwatch$ or band or bands or wristband$ or tracker$1 or cloth$ or garment$ or textile$ or jewellery or bracelet$)).ti,kw. (2370)
56 wearable$1.ti,kw. (3139)
57 (android$ or ios).ti,kw. (597)
58 apple$.ti,kw. (7190)
59 (AliveCor$ or AliveECG$ or Kardia Mobile$ or iTransmit or search-AF or GP-search or iECG$ or ChoiceMMed$ or Beijing Choice$ or MD100E$ or MD-100E$ or MD100-E$ or MD100B$ or MD-100B$ or MD100-B$ or Easy ECG$ or EasyECG$ or Creative Medical$ or Shenzhen Creative$ or Heal Force$ or HealForce$ or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or

PC-80b or Prince-180b or Prince180b or heartscan$ or HCG-801 or HCG801 or dimetek$ or diCare$ or mc1cc or mc1c or m1ca or m1cb or blade micro or mono micro or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics$ or AfibAlert$ or Lohman Tech$ or cardio24$ or mednovis$ or instantcheck$ or readmyheart$ or dailycare biomedical$ or daily care biomedical$ or dc biomed$ or dcbiomed$ or ecgcheck$ or ecg check$ or cardiac designs$ or MyDiagnostick$ or Applied Biomedical Systems$ or Qardio$ or VitalPatch$ or VitalConnect$ or Beat2Phone$ or Beat 2 Phone$ or VitalSygum$ or Vital Sygum$).ti,kw,dv,dm. (121)
60 (contec$ and (pm-10 or pm10 or pm-80 or pm80)).ti,kw,dv,dm. (0)
61 (heartcheck$ or (ecg adj3 pen)).ti,kw,dv,dm. (5)
62 (beurer$ and (ME-80 or ME-90 or ME80 or ME90)).ti,kw,dv,dm. (0)
63 (reka and e100$).ti,kw,dv,dm. (2)
64 *non invasive measurement/ or ((noninvasiv$ or non-invasiv$) adj4 (monitor$ or measur$ or determin$ or assess$ or evaluat$)).ti,kw. (14058)
65 or/11-64 (236551)
66 5 and 10 (3766)
67 5 and 65 (5534)
68 66 or 67 (8626)
69 exp "sensitivity and specificity"/ (285888)
70 sensitivity.tw. (867245)
71 specificity.tw. (507897)
72 ((pre-test or pretest) adj probability).tw. (3149)
73 post-test probability.tw. (673)
74 predictive value$.tw. (132762)
75 likelihood ratio$.tw. (16987)
76 *Diagnostic Accuracy/ (8581)
77 or/69-76 (1313603)
78 diagnostic test accuracy study/ or (diagnos$ adj5 accurac$).ti,ab,kw. (130628)
79 ((posttest or postest) adj probabilit$).ti,ab,kw. (399)
80 (false positive$1 or false negative$1 or true positive$1).ti,ab,kw. (94018)
81 receiver operating characteristic/ or exp diagnostic error/ or observer variation/ (182519)
82 roc curve$.ti,ab,kw. (44108)
83 receiver operating characteristic.ti,ab,kw. (55204)
84 observer variation$.ti,ab,kw. (1930)
85 or/78-84 (373196)
86 77 or 85 (1518473)
87 68 and 86 (1721)
88 5 and ((test or tests or tested or testing or screen or detect$) adj5 accura$).ti,ab,kw. (442)
89 87 or 88 (1985)
90 "systematic review"/ or "systematic review (topic)"/ (177515)

91 meta analysis/ or "meta analysis (topic)"/ (172073)
92 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kw. (296366)
93 or/90-92 (393084)
94 68 and 93 (148)
95 Health Economics/ (35517)
96 exp Economic Evaluation/ (268970)
97 exp Health Care Cost/ (257956)
98 pharmacoeconomics/ (7787)
99 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (861268)
100 (expenditure$ not energy).ti,ab. (33394)
101 (value adj2 money).ti,ab. (2038)
102 budget$.ti,ab. (32397)
103 or/95-102 (1103147)
104 (metabolic adj cost).ti,ab. (1280)
105 ((energy or oxygen) adj cost).ti,ab. (3830)
106 ((energy or oxygen) adj expenditure).ti,ab. (27435)
107 or/104-106 (31553)
108 103 not 107 (1096662)
109 biomedical technology assessment/ (12566)
110 (technology assessment$ or technology appraisal$ or hta or htas).ti,ab,kw. (10869)
111 economic model/ or statistical model/ (147988)
112 econometric$.ti,ab,kw. (1679)
113 or/109-112 (170062)
114 108 or 113 (1242266)
115 68 and 114 (470)
116 Randomized controlled trial/ (488152)
117 randomization/ (77137)
118 (random$ or placebo).ti,ab,kw. (1371116)
119 or/116-118 (1476595)
120 68 and 119 (640)
121 89 or 115 or 120 (2778)
122 United Kingdom/ (387737)
123 (national health service* or nhs*).ti,ab,in,ad. (273558)
124 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (34253)

125 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in,ad. (2840530)

126 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in,ad. (2118019)

127 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in,ad. (85531)

128 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in,ad. (293553)

129 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in,ad. (38507)

130 or/122-129 (3463810)

131 (exp "arctic and antarctic"/ or exp oceanic regions/ or exp western hemisphere/ or exp africa/ or exp asia/ or exp "australia and new zealand"/) not (united kingdom/ or europe/) (2768111)

132 130 not 131 (3286006)

133 exp United States/ (1161170)

134 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,kw,jw,ad. (9253197)

135 exp Europe/ or european union/ (1490500)
136 (europe$ or eu or "eu's" or "e.u." or 5eu or eu5).ti,ab,kw,jw,ad. (1231683)
137 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kw,jw,ad. (7998088)
138 exp Canada/ (163346)
139 (canada$ or canadian$).ti,ab,kw,jw,ad. (980799)
140 exp "Australia and New Zealand"/ (199384)
141 (australia$ or australas$).ti,ab,kw,jw,ad. (710107)
142 new zealand$.ti,ab,kw,jw,ad. (174061)
143 or/133-142 (19517466)
144 132 or 143 (21253735)
145 121 and 144 (2244)
146 94 or 145 (2311)
147 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5802481)
148 editorial.pt. or case report.ti. (812292)
149 conference abstract.pt. (2889809)
150 146 not (147 or 148 or 149) (1449)
151 limit 150 to (english language and yr="2011 -Current") (677)
152 remove duplicates from 151 (644)
153 from 152 keep 1-644 (644)

Source: Database of Abstracts of Reviews of Effects: Issue 2 of 4, April 2015
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 23/02/18
Retrieved records: 12
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11032
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134
#5 #1 or #2 or #3 or #4 17669
#6 [mh ^"Mass Screening"] 4916

#7 screen*:ti 9454
#8 (test or tests or tested or testing):ti 16448
#9 detect*:ti 7111
#10 #6 or #7 or #8 or #9 32112
#11 [mh ^Pulse] 1430
#12 (pulse or pulses):ti 1662
#13 [mh ^Photoplethysmography] 84
#14 (photoplethysmogra* or photo-plethysmogra* or photoreflexometr* or photo-reflexometr* or light next reflection next rheogra* or photoelectric next plethysmogra* or ppg or ppgs):ti 39
#15 [mh ^"Blood Pressure Monitors"] 164
#16 [mh ^"Blood Pressure Determination"/is] 158
#17 ((blood next pressure* or bp) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1131
#18 sphygmomanometer*:ti 45
#19 [mh ^Electrocardiography] 7603
#20 [mh ^"Electrocardiography, Ambulatory"] 1170
#21 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph*):ti 1067
#22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs):ti 557
#23 (holter* next monitor*):ti 75
#24 [mh ^"monitoring, ambulatory"] or [mh ^"blood pressure monitoring, ambulatory"] 1943
#25 ((ambulatory or portable or pocket*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 764
#26 ((outpatient* or out-patient* or home* or remot*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1515
#27 (self near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1494
#28 [mh ^"Cell Phones"] 566
#29 (m-health* or mhealth* or mobile next health*):ti 250
#30 ((mobile or smart or cell or cellular) near/3 (phone* or telephone* or handset* or hand-set*)):ti 529
#31 mobiles:ti 0
#32 ((hand or handheld) near/3 (phone* or telephone*)):ti 2
#33 smartphone*:ti 350
#34 (iphone* or i-phone*):ti 13
#35 [mh ^"Computers, Handheld"] 220
#36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) near/3 (comput* or PC or PCs or system or systems)):ti 115
#37 (mobile near/3 (communicat* or technology or technologies or network*)):ti 91

#38 ((mobile or electronic* or digital* or device* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 tablet*):ti 14
#39 (tablet* near/3 (comput* or PC or PCs or device or devices)):ti 54
#40 (phablet* or slate or slates or laplet* or mini-tablet* or hybrid next tablet* or convertible next tablet*):ti 8
#41 (booklet* and tablet*):ti 0
#42 ((mobile or electronic* or digital* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 (device or devices)):ti 241
#43 (personal next digital next assistant*):ti 31
#44 ((PDA or PDAs) not ("ductus arteriosus" or posterior next descending next arter* or pancreatic next ductal next adenocarcinoma*)):ti 70
#45 (device-based or mobile-based):ti 49
#46 ((device* or mobile) near/2 technolog*):ti 94
#47 (smart next (digital* or device* or technolog*)):ti 4
#48 (ipad* or i-pad* or ipod* or i-pod*):ti 70
#49 [mh ^"Mobile Applications"] 216
#50 (app or apps):ti 203
#51 ((mobile or phone* or telephone* or device* or tablet* or electronic* or digital* or software*) near/3 application*):ti 175
#52 [mh ^"Wireless Technology"] or ((wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*) and (mobile or phone* or telephone* or tablet*)):ti 45
#53 (ubiquitous and (mobile or phone* or telephone* or device or devices or tablet* or wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*)):ti 3
#54 smartwatch*:ti 4
#55 ((mobile or electronic* or digital* or digitis* or digitiz* or wireless* or smart) near/3 (patch or patches or monitor* or watch or watches or wristwatch* or band or bands or wristband* or tracker* or cloth* or garment* or textile* or jewellery or bracelet*)):ti 225
#56 wearable*:ti 96
#57 (android* or ios):ti 36
#58 apple*:ti 200
#59 (AliveCor* or AliveECG* or Kardia next Mobile* or iTransmit or search-AF or GP-search or iECG* or ChoiceMMed* or Beijing next Choice* or MD100E* or MD-100E* or MD100-E* or MD100B* or MD-100B* or MD100-B* or Easy next ECG* or EasyECG* or Creative next Medical* or Shenzhen next Creative* or Heal next Force* or HealForce* or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan* or HCG-801 or HCG801 or dimetek* or diCare* or mc1cc or mc1c or m1ca or m1cb or "blade micro" or "mono micro" or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics* or AfibAlert* or Lohman next Tech* or cardio24* or mednovis* or instantcheck* or readmyheart* or dailycare next biomedical* or daily next care next biomedical* or dc next biomed* or dcbiomed* or ecgcheck* or ecg next check* or cardiac next designs* or MyDiagnostick* or Applied next Biomedical next Systems* or

Qardio* or VitalPatch* or VitalConnect* or Beat2Phone* or Beat next 2 next Phone* or VitalSygum* or Vital next Sygum*):ti 5
#60 (contec* and (pm-10 or pm10 or pm-80 or pm80)):ti 0
#61 (heartcheck* or (ecg near/3 pen)):ti 0
#62 (beurer* and (ME-80 or ME-90 or ME80 or ME90)):ti 0
#63 (reka and e100*):ti 0
#64 ((noninvasiv* or non-invasiv*) near/4 (monitor* or measur* or determin* or assess* or evaluat*)):ti 499
#65 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 21217
#66 #5 and #10 473
#67 #5 and #65 1215
#68 #66 or #67 1583
#69 #68 Publication Year from 2011 to 2018 696
#70 #69 in Other Reviews 12

Source: Health Technology Assessment Database: Issue 4 of 4, October 2016
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 23/02/18
Retrieved records: 7
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11032
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134
#5 #1 or #2 or #3 or #4 17669
#6 [mh ^"Mass Screening"] 4916
#7 screen*:ti 9454
#8 (test or tests or tested or testing):ti 16448
#9 detect*:ti 7111
#10 #6 or #7 or #8 or #9 32112
#11 [mh ^Pulse] 1430
#12 (pulse or pulses):ti 1662
#13 [mh ^Photoplethysmography] 84

#14 (photoplethysmogra* or photo-plethysmogra* or photoreflexometr* or photo-reflexometr* or light next reflection next rheogra* or photoelectric next plethysmogra* or ppg or ppgs):ti 39
#15 [mh ^"Blood Pressure Monitors"] 164
#16 [mh ^"Blood Pressure Determination"/is] 158
#17 ((blood next pressure* or bp) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1131
#18 sphygmomanometer*:ti 45
#19 [mh ^Electrocardiography] 7603
#20 [mh ^"Electrocardiography, Ambulatory"] 1170
#21 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph*):ti 1067
#22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs):ti 557
#23 (holter* next monitor*):ti 75
#24 [mh ^"monitoring, ambulatory"] or [mh ^"blood pressure monitoring, ambulatory"] 1943
#25 ((ambulatory or portable or pocket*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 764
#26 ((outpatient* or out-patient* or home* or remot*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1515
#27 (self near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1494
#28 [mh ^"Cell Phones"] 566
#29 (m-health* or mhealth* or mobile next health*):ti 250
#30 ((mobile or smart or cell or cellular) near/3 (phone* or telephone* or handset* or hand-set*)):ti 529
#31 mobiles:ti 0
#32 ((hand or handheld) near/3 (phone* or telephone*)):ti 2
#33 smartphone*:ti 350
#34 (iphone* or i-phone*):ti 13
#35 [mh ^"Computers, Handheld"] 220
#36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) near/3 (comput* or PC or PCs or system or systems)):ti 115
#37 (mobile near/3 (communicat* or technology or technologies or network*)):ti 91
#38 ((mobile or electronic* or digital* or device* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 tablet*):ti 14
#39 (tablet* near/3 (comput* or PC or PCs or device or devices)):ti 54
#40 (phablet* or slate or slates or laplet* or mini-tablet* or hybrid next tablet* or convertible next tablet*):ti 8
#41 (booklet* and tablet*):ti 0
#42 ((mobile or electronic* or digital* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 (device or devices)):ti 241

#43 (personal next digital next assistant*):ti 31
#44 ((PDA or PDAs) not ("ductus arteriosus" or posterior next descending next arter* or pancreatic next ductal next adenocarcinoma*)):ti 70
#45 (device-based or mobile-based):ti 49
#46 ((device* or mobile) near/2 technolog*):ti 94
#47 (smart next (digital* or device* or technolog*)):ti 4
#48 (ipad* or i-pad* or ipod* or i-pod*):ti 70
#49 [mh ^"Mobile Applications"] 216
#50 (app or apps):ti 203
#51 ((mobile or phone* or telephone* or device* or tablet* or electronic* or digital* or software*) near/3 application*):ti 175
#52 [mh ^"Wireless Technology"] or ((wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*) and (mobile or phone* or telephone* or tablet*)):ti 45
#53 (ubiquitous and (mobile or phone* or telephone* or device or devices or tablet* or wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*)):ti 3
#54 smartwatch*:ti 4
#55 ((mobile or electronic* or digital* or digitis* or digitiz* or wireless* or smart) near/3 (patch or patches or monitor* or watch or watches or wristwatch* or band or bands or wristband* or tracker* or cloth* or garment* or textile* or jewellery or bracelet*)):ti 225
#56 wearable*:ti 96
#57 (android* or ios):ti 36
#58 apple*:ti 200
#59 (AliveCor* or AliveECG* or Kardia next Mobile* or iTransmit or search-AF or GP-search or iECG* or ChoiceMMed* or Beijing next Choice* or MD100E* or MD-100E* or MD100-E* or MD100B* or MD-100B* or MD100-B* or Easy next ECG* or EasyECG* or Creative next Medical* or Shenzhen next Creative* or Heal next Force* or HealForce* or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan* or HCG-801 or HCG801 or dimetek* or diCare* or mc1cc or mc1c or m1ca or m1cb or "blade micro" or "mono micro" or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics* or AfibAlert* or Lohman next Tech* or cardio24* or mednovis* or instantcheck* or readmyheart* or dailycare next biomedical* or daily next care next biomedical* or dc next biomed* or dcbiomed* or ecgcheck* or ecg next check* or cardiac next designs* or MyDiagnostick* or Applied next Biomedical next Systems* or Qardio* or VitalPatch* or VitalConnect* or Beat2Phone* or Beat next 2 next Phone* or VitalSygum* or Vital next Sygum*):ti 5
#60 (contec* and (pm-10 or pm10 or pm-80 or pm80)):ti 0
#61 (heartcheck* or (ecg near/3 pen)):ti 0
#62 (beurer* and (ME-80 or ME-90 or ME80 or ME90)):ti 0
#63 (reka and e100*):ti 0
#64 ((noninvasiv* or non-invasiv*) near/4 (monitor* or measur* or determin* or assess* or evaluat*)):ti 499

#65 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 21217
#66 #5 and #10 473
#67 #5 and #65 1215
#68 #66 or #67 1583
#69 #68 Publication Year from 2011 to 2018 696
#70 #69 in Other Reviews 12
#71 #69 in Technology Assessments 7

Source: NHS Economic Evaluation Database: Issue 2 of 4, April 2015
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 23/02/18
Retrieved records: 7
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11032
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134
#5 #1 or #2 or #3 or #4 17669
#6 [mh ^"Mass Screening"] 4916
#7 screen*:ti 9454
#8 (test or tests or tested or testing):ti 16448
#9 detect*:ti 7111
#10 #6 or #7 or #8 or #9 32112
#11 [mh ^Pulse] 1430
#12 (pulse or pulses):ti 1662
#13 [mh ^Photoplethysmography] 84
#14 (photoplethysmogra* or photo-plethysmogra* or photoreflexometr* or photo-reflexometr* or light next reflection next rheogra* or photoelectric next plethysmogra* or ppg or ppgs):ti 39
#15 [mh ^"Blood Pressure Monitors"] 164
#16 [mh ^"Blood Pressure Determination"/is] 158
#17 ((blood next pressure* or bp) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1131
#18 sphygmomanometer*:ti 45
#19 [mh ^Electrocardiography] 7603

#20 [mh ^"Electrocardiography, Ambulatory"] 1170
#21 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph*):ti 1067
#22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs):ti 557
#23 (holter* next monitor*):ti 75
#24 [mh ^"monitoring, ambulatory"] or [mh ^"blood pressure monitoring, ambulatory"] 1943
#25 ((ambulatory or portable or pocket*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 764
#26 ((outpatient* or out-patient* or home* or remot*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1515
#27 (self near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1494
#28 [mh ^"Cell Phones"] 566
#29 (m-health* or mhealth* or mobile next health*):ti 250
#30 ((mobile or smart or cell or cellular) near/3 (phone* or telephone* or handset* or hand-set*)):ti 529
#31 mobiles:ti 0
#32 ((hand or handheld) near/3 (phone* or telephone*)):ti 2
#33 smartphone*:ti 350
#34 (iphone* or i-phone*):ti 13
#35 [mh ^"Computers, Handheld"] 220
#36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) near/3 (comput* or PC or PCs or system or systems)):ti 115
#37 (mobile near/3 (communicat* or technology or technologies or network*)):ti 91
#38 ((mobile or electronic* or digital* or device* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 tablet*):ti 14
#39 (tablet* near/3 (comput* or PC or PCs or device or devices)):ti 54
#40 (phablet* or slate or slates or laplet* or mini-tablet* or hybrid next tablet* or convertible next tablet*):ti 8
#41 (booklet* and tablet*):ti 0
#42 ((mobile or electronic* or digital* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 (device or devices)):ti 241
#43 (personal next digital next assistant*):ti 31
#44 ((PDA or PDAs) not ("ductus arteriosus" or posterior next descending next arter* or pancreatic next ductal next adenocarcinoma*)):ti 70
#45 (device-based or mobile-based):ti 49
#46 ((device* or mobile) near/2 technolog*):ti 94
#47 (smart next (digital* or device* or technolog*)):ti 4
#48 (ipad* or i-pad* or ipod* or i-pod*):ti 70
#49 [mh ^"Mobile Applications"] 216
#50 (app or apps):ti 203

#51 ((mobile or phone* or telephone* or device* or tablet* or electronic* or digital* or software*) near/3 application*):ti 175
#52 [mh ^"Wireless Technology"] or ((wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*) and (mobile or phone* or telephone* or tablet*)):ti 45
#53 (ubiquitous and (mobile or phone* or telephone* or device or devices or tablet* or wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*)):ti 3
#54 smartwatch*:ti 4
#55 ((mobile or electronic* or digital* or digitis* or digitiz* or wireless* or smart) near/3 (patch or patches or monitor* or watch or watches or wristwatch* or band or bands or wristband* or tracker* or cloth* or garment* or textile* or jewellery or bracelet*)):ti 225
#56 wearable*:ti 96
#57 (android* or ios):ti 36
#58 apple*:ti 200
#59 (AliveCor* or AliveECG* or Kardia next Mobile* or iTransmit or search-AF or GP-search or iECG* or ChoiceMMed* or Beijing next Choice* or MD100E* or MD-100E* or MD100-E* or MD100B* or MD-100B* or MD100-B* or Easy next ECG* or EasyECG* or Creative next Medical* or Shenzhen next Creative* or Heal next Force* or HealForce* or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan* or HCG-801 or HCG801 or dimetek* or diCare* or mc1cc or mc1c or m1ca or m1cb or "blade micro" or "mono micro" or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics* or AfibAlert* or Lohman next Tech* or cardio24* or mednovis* or instantcheck* or readmyheart* or dailycare next biomedical* or daily next care next biomedical* or dc next biomed* or dcbiomed* or ecgcheck* or ecg next check* or cardiac next designs* or MyDiagnostick* or Applied next Biomedical next Systems* or Qardio* or VitalPatch* or VitalConnect* or Beat2Phone* or Beat next 2 next Phone* or VitalSygum* or Vital next Sygum*):ti 5
#60 (contec* and (pm-10 or pm10 or pm-80 or pm80)):ti 0
#61 (heartcheck* or (ecg near/3 pen)):ti 0
#62 (beurer* and (ME-80 or ME-90 or ME80 or ME90)):ti 0
#63 (reka and e100*):ti 0
#64 ((noninvasiv* or non-invasiv*) near/4 (monitor* or measur* or determin* or assess* or evaluat*)):ti 499
#65 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 21217
#66 #5 and #10 473
#67 #5 and #65 1215
#68 #66 or #67 1583
#69 #68 Publication Year from 2011 to 2018 696

#70 #69 in Other Reviews 12
#71 #69 in Technology Assessments 7
#72 #69 in Economic Evaluations 7

Source: Cochrane Database of Systematic Reviews: Issue 2 of 12, February 2018
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 23/02/18
Retrieved records: 2
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)):ti,ab,kw 9805
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib):ti,ab,kw 4611
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib):ti,ab,kw 130
#5 #1 or #2 or #3 or #4 10888
#6 [mh ^"Mass Screening"] 4916
#7 screen*:ti 9454
#8 (test or tests or tested or testing):ti 16448
#9 detect*:ti 7111
#10 #6 or #7 or #8 or #9 32112
#11 [mh ^Pulse] 1430
#12 (pulse or pulses):ti 1662
#13 [mh ^Photoplethysmography] 84
#14 (photoplethysmogra* or photo-plethysmogra* or photoreflexometr* or photo-reflexometr* or light next reflection next rheogra* or photoelectric next plethysmogra* or ppg or ppgs):ti 39
#15 [mh ^"Blood Pressure Monitors"] 164
#16 [mh ^"Blood Pressure Determination"/is] 158
#17 ((blood next pressure* or bp) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1131
#18 sphygmomanometer*:ti 45
#19 [mh ^Electrocardiography] 7603
#20 [mh ^"Electrocardiography, Ambulatory"] 1170
#21 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph*):ti 1067
#22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs):ti 557
#23 (holter* next monitor*):ti 75
#24 [mh ^"monitoring, ambulatory"] or [mh ^"blood pressure monitoring, ambulatory"] 1943

#25 ((ambulatory or portable or pocket*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 764
#26 ((outpatient* or out-patient* or home* or remot*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1515
#27 (self near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1494
#28 [mh ^"Cell Phones"] 566
#29 (m-health* or mhealth* or mobile next health*):ti 250
#30 ((mobile or smart or cell or cellular) near/3 (phone* or telephone* or handset* or hand-set*)):ti 529
#31 mobiles:ti 0
#32 ((hand or handheld) near/3 (phone* or telephone*)):ti 2
#33 smartphone*:ti 350
#34 (iphone* or i-phone*):ti 13
#35 [mh ^"Computers, Handheld"] 220
#36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) near/3 (comput* or PC or PCs or system or systems)):ti 115
#37 (mobile near/3 (communicat* or technology or technologies or network*)):ti 91
#38 ((mobile or electronic* or digital* or device* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 tablet*):ti 14
#39 (tablet* near/3 (comput* or PC or PCs or device or devices)):ti 54
#40 (phablet* or slate or slates or laplet* or mini-tablet* or hybrid next tablet* or convertible next tablet*):ti 8
#41 (booklet* and tablet*):ti 0
#42 ((mobile or electronic* or digital* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 (device or devices)):ti 241
#43 (personal next digital next assistant*):ti 31
#44 ((PDA or PDAs) not ("ductus arteriosus" or posterior next descending next arter* or pancreatic next ductal next adenocarcinoma*)):ti 70
#45 (device-based or mobile-based):ti 49
#46 ((device* or mobile) near/2 technolog*):ti 94
#47 (smart next (digital* or device* or technolog*)):ti 4
#48 (ipad* or i-pad* or ipod* or i-pod*):ti 70
#49 [mh ^"Mobile Applications"] 216
#50 (app or apps):ti 203
#51 ((mobile or phone* or telephone* or device* or tablet* or electronic* or digital* or software*) near/3 application*):ti 175
#52 [mh ^"Wireless Technology"] or ((wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*) and (mobile or phone* or telephone* or tablet*)):ti 45
#53 (ubiquitous and (mobile or phone* or telephone* or device or devices or tablet* or wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*)):ti 3
#54 smartwatch*:ti 4

#55 ((mobile or electronic* or digital* or digitis* or digitiz* or wireless* or smart) near/3 (patch or patches or monitor* or watch or watches or wristwatch* or band or bands or wristband* or tracker* or cloth* or garment* or textile* or jewellery or bracelet*)):ti 225
#56 wearable*:ti 96
#57 (android* or ios):ti 36
#58 apple*:ti 200
#59 (AliveCor* or AliveECG* or Kardia next Mobile* or iTransmit or search-AF or GP-search or iECG* or ChoiceMMed* or Beijing next Choice* or MD100E* or MD-100E* or MD100-E* or MD100B* or MD-100B* or MD100-B* or Easy next ECG* or EasyECG* or Creative next Medical* or Shenzhen next Creative* or Heal next Force* or HealForce* or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan* or HCG-801 or HCG801 or dimetek* or diCare* or mc1cc or mc1c or m1ca or m1cb or "blade micro" or "mono micro" or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics* or AfibAlert* or Lohman next Tech* or cardio24* or mednovis* or instantcheck* or readmyheart* or dailycare next biomedical* or daily next care next biomedical* or dc next biomed* or dcbiomed* or ecgcheck* or ecg next check* or cardiac next designs* or MyDiagnostick* or Applied next Biomedical next Systems* or Qardio* or VitalPatch* or VitalConnect* or Beat2Phone* or Beat next 2 next Phone* or VitalSygum* or Vital next Sygum*):ti 5
#60 (contec* and (pm-10 or pm10 or pm-80 or pm80)):ti 0
#61 (heartcheck* or (ecg near/3 pen)):ti 0
#62 (beurer* and (ME-80 or ME-90 or ME80 or ME90)):ti 0
#63 (reka and e100*):ti 0
#64 ((noninvasiv* or non-invasiv*) near/4 (monitor* or measur* or determin* or assess* or evaluat*)):ti 499
#65 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 21217
#66 #5 and #10 281
#67 #5 and #65 1094
#68 #66 or #67 1274
#69 #68 Publication Year from 2011 to 2018 568
#70 #69 in Cochrane Reviews (Reviews and Protocols) 2

Source: Cochrane Central Register of Controlled Trials: Issue 1 of 12, January 2018

Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 23/02/18

Retrieved records: 553
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3577
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10360
#3 (A-Fib or AFib or PAF or PA-Fib or PAFib) or AF:ti,ab,kw 4653
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 134
#5 #1 or #2 or #3 or #4 11474
#6 [mh ^"Mass Screening"] 4916
#7 screen*:ti 9454
#8 (test or tests or tested or testing):ti 16448
#9 detect*:ti 7111
#10 #6 or #7 or #8 or #9 32112
#11 [mh ^Pulse] 1430
#12 (pulse or pulses):ti 1662
#13 [mh ^Photoplethysmography] 84
#14 (photoplethysmogra* or photo-plethysmogra* or photoreflexometr* or photo-reflexometr* or light next reflection next rheogra* or photoelectric next plethysmogra* or ppg or ppgs):ti 39
#15 [mh ^"Blood Pressure Monitors"] 164
#16 [mh ^"Blood Pressure Determination"/is] 158
#17 ((blood next pressure* or bp) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1131
#18 sphygmomanometer*:ti 45
#19 [mh ^Electrocardiography] 7603
#20 [mh ^"Electrocardiography, Ambulatory"] 1170
#21 (electrocardiogram* or cardiogram* or electrocardiograph* or cardiograph*):ti 1067
#22 (ecg or ecgs or iecg or iecgs or ekg or ekgs or iekg or iekgs):ti 557
#23 (holter* next monitor*):ti 75
#24 [mh ^"monitoring, ambulatory"] or [mh ^"blood pressure monitoring, ambulatory"] 1943
#25 ((ambulatory or portable or pocket*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 764
#26 ((outpatient* or out-patient* or home* or remot*) near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1515
#27 (self near/5 (monitor* or measur* or determin* or assess* or evaluat*)):ti 1494
#28 [mh ^"Cell Phones"] 566
#29 (m-health* or mhealth* or mobile next health*):ti 250
#30 ((mobile or smart or cell or cellular) near/3 (phone* or telephone* or handset* or hand-set*)):ti 529

#31 mobiles:ti 0
#32 ((hand or handheld) near/3 (phone* or telephone*)):ti 2
#33 smartphone*:ti 350
#34 (iphone* or i-phone*):ti 13
#35 [mh ^"Computers, Handheld"] 220
#36 ((mobile or handheld or hand-held or pocket or palm or palmtop or portable) near/3 (comput* or PC or PCs or system or systems)):ti 115
#37 (mobile near/3 (communicat* or technology or technologies or network*)):ti 91
#38 ((mobile or electronic* or digital* or device* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 tablet*):ti 14
#39 (tablet* near/3 (comput* or PC or PCs or device or devices)):ti 54
#40 (phablet* or slate or slates or laplet* or mini-tablet* or hybrid next tablet* or convertible next tablet*):ti 8
#41 (booklet* and tablet*):ti 0
#42 ((mobile or electronic* or digital* or portable or pocket* or handheld or hand-held or palm or palmtop) near/3 (device or devices)):ti 241
#43 (personal next digital next assistant*):ti 31
#44 ((PDA or PDAs) not ("ductus arteriosus" or posterior next descending next arter* or pancreatic next ductal next adenocarcinoma*)):ti 70
#45 (device-based or mobile-based):ti 49
#46 ((device* or mobile) near/2 technolog*):ti 94
#47 (smart next (digital* or device* or technolog*)):ti 4
#48 (ipad* or i-pad* or ipod* or i-pod*):ti 70
#49 [mh ^"Mobile Applications"] 216
#50 (app or apps):ti 203
#51 ((mobile or phone* or telephone* or device* or tablet* or electronic* or digital* or software*) near/3 application*):ti 175
#52 [mh ^"Wireless Technology"] or ((wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*) and (mobile or phone* or telephone* or tablet*)):ti 45
#53 (ubiquitous and (mobile or phone* or telephone* or device or devices or tablet* or wireless or wire-less or wifi or wi-fi or bluetooth* or blue-tooth*)):ti 3
#54 smartwatch*:ti 4
#55 ((mobile or electronic* or digital* or digitis* or digitiz* or wireless* or smart) near/3 (patch or patches or monitor* or watch or watches or wristwatch* or band or bands or wristband* or tracker* or cloth* or garment* or textile* or jewellery or bracelet*)):ti 225
#56 wearable*:ti 96
#57 (android* or ios):ti 36
#58 apple*:ti 200
#59 (AliveCor* or AliveECG* or Kardia next Mobile* or iTransmit or search-AF or GP-search or iECG* or ChoiceMMed* or Beijing next Choice* or MD100E* or MD-100E* or MD100-E* or MD100B* or MD-100B* or MD100-B* or Easy next ECG* or EasyECG* or

Creative next Medical* or Shenzhen next Creative* or Heal next Force* or HealForce* or PC80 or PC-80 or Prince-180 or Prince180 or PC80a or PC-80a or Prince-180a or Prince180a or PC80b or PC-80b or Prince-180b or Prince180b or heartscan* or HCG-801 or HCG801 or dimetek* or diCare* or mc1cc or mc1c or m1ca or m1cb or "blade micro" or "mono micro" or ecg-80A or ekg-80A or ecg-90A or ekg-90A or ecg80A or ekg80A or ecg90A or ekg90A or BodiMetrics* or AfibAlert* or Lohman next Tech* or cardio24* or mednovis* or instantcheck* or readmyheart* or dailycare next biomedical* or daily next care next biomedical* or dc next biomed* or dcbiomed* or ecgcheck* or ecg next check* or cardiac next designs* or MyDiagnostick* or Applied next Biomedical next Systems* or Qardio* or VitalPatch* or VitalConnect* or Beat2Phone* or Beat next 2 next Phone* or VitalSygum* or Vital next Sygum*):ti 5

#60 (contec* and (pm-10 or pm10 or pm-80 or pm80)):ti 0

#61 (heartcheck* or (ecg near/3 pen)):ti 0

#62 (beurer* and (ME-80 or ME-90 or ME80 or ME90)):ti 0

#63 (reka and e100*):ti 0

#64 ((noninvasiv* or non-invasiv*) near/4 (monitor* or measur* or determin* or assess* or evaluat*)):ti 499

#65 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 21217

#66 #5 and #10 294

#67 #5 and #65 1113

#68 #66 or #67 1306

#69 #68 Publication Year from 2011 to 2018 583

#70 #69 in Trials 553

Source: Cost-Effectiveness Analysis (CEA) Registry

Interface / URL: http://healtheconomics.tuftsmedicalcenter.org/cear4/home.aspx

Database coverage dates: Not given

Search date: 23/3/18

Retrieved records: 102

Search strategy:

The source was searched using the search interface at: http://healtheconomics.tuftsmedicalcenter.org/cear4/SearchingtheCEARegistry/SearchtheCEARegistry.aspx. The basic search interface was used (standard access).

Note:

- The CEA Registry has very limited search functionality.

- Due to the limited functionality it was not possible to search efficiently on the search term 'AF'. The term was therefore not searched on.
- Using standard access, only the first 100 results of those returned were accessible for retrieval

The following terms were searched on individually ('Articles' selected). Returned results published from 2011 to date were copied into a Word document. Where more than 100 results were returned, only the first 100 results were retrieved (see note above).

Atrial fibrillation = 100 (146 results returned, 100 accessible)
Atrial tachycardia = 0 (1 result returned, excluded as pre-2011)
Atrial tachycardias = 0 (0 results returned)
Atrial tachyarrhythmia = 0 (1 result returned, excluded as pre-2011)
Atrial tachyarrhythmias = 0 (1 result returned, excluded as pre-2011)
Atrium = 0 (1 result returned, excluded as pre-2011)
Auricular = 0 (1 result returned, excluded as pre-2011)
Heart fibrillation = 0 (0 results returned)
Heart tachycardia = 0 (0 results returned)
Heart tachycardias = 0 (0 results returned)
Heart tachyarrhythmia = 0 (0 results returned)
Heart tachyarrhythmias = 0 (0 results returned)
Cardiac fibrillation = 0 (0 results returned)
Cardiac tachycardia = 0 (0 results returned)
Cardiac tachycardias = 0 (0 results returned)
Cardiac tachyarrhythmia = 0 (0 results returned)
Cardiac tachyarrhythmias = 0 (0 results returned)
A-Fib = 0 (0 results returned)
AFib = 0 (0 results returned)
PAF = 1 (5 results returned, 4 excluded as duplicates of results already retrieved from this source)
PA-Fib = 0 (0 results returned)
PAFib = 0 (0 results returned)
NVAF = 1 (16 results returned, 1 excluded as pre-2011, 14 excluded as duplicates of results already retrieved from this source)
NVA-Fib = 0 (0 results returned)
NVAFib = 0 (0 results returned)
NVPAF = 0 (0 results returned)
NVPA-Fib = 0 (0 results returned)
NVPAFib = 0 (0 results returned)

SEARCH 3: RESEARCH QUESTIONS 2 and 6

Source: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Interface / URL: OvidSP
Database coverage dates: 1946 to Present
Search date: 23/02/18
Retrieved records: 1946
Search strategy:

1 *Atrial Fibrillation/ (36693)
2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kf. (65867)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kf. (42798)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kf. (683)
5 or/1-4 (91419)
6 apixaban$.ti,ab,kf,rn,nm. (2439)
7 (bms 562247 or bms562247 or eliques$2 or eliquis$2).ti,ab,kf,rn,nm. (52)
8 (503612-47-3 or 3Z9Y7UWC1J).ti,ab,kf,rn,nm. (1104)
9 Dabigatran/ (2292)
10 (dabigatran$ or bibr 1048 or bibr1048 or pradaxa$2 or pradax$2 or prazaxa$2 or rendix$2).ti,ab,kf,rn,nm. (4167)
11 (211915-06-9 or I0VM4M70GC).ti,ab,kf,rn,nm. (2292)
12 Rivaroxaban/ (2001)
13 rivaroxaban$.ti,ab,kf,rn,nm. (3850)
14 (bay 59 7939 or bay 597939 or bay59 7939 or bay597939 or xarelto$2).ti,ab,kf,rn,nm. (142)
15 (366789-02-8 or 9NDF7JZ4M3).ti,ab,kf,rn,nm. (2001)
16 edoxaban$.ti,ab,kf,rn,nm. (961)
17 (du 176 or du 176b or du176 or du176b or lixiana$2 or savaysa$2 or endoxaban$2 or roteas$2).ti,ab,kf,rn,nm. (47)
18 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO).ti,ab,kf,rn,nm. (374)
19 exp Vitamin K/ai [Antagonists & Inhibitors] (2358)
20 ((vitamin k or vitamins k) adj3 (antagonist$1 or inhibitor$1 or blocker$1)).ti,ab,kf,rn,nm. (4858)
21 (anti vitamin k or antivitamin k or anti vitamins k or antivitamins k or menadione antagonist$1).ti,ab,kf,rn,nm. (484)
22 (vka or vkas).ti,ab,kf,rn,nm. (1581)
23 Warfarin/ (17516)
24 warfarin$.ti,ab,kf,rn,nm. (26988)
25 (acetonylbenzylhydroxycoumarin$2 or adoisine$2 or aldocumar$2 or antrombin k$2 or athrombin$2 or athrombine$2 or athrombinek$2 or befarin$2 or carfin$2 or circuvit$2

or compound 42$2 or coumadan$ or coumadin$2 or coumadine$2 or coumafene$2 or coumaphene$2 or dagonal$2 or farin$2 or hydroxycoumarin$2 or jantoven$2 or kumatox$2 or maforan$2 or marevan$2 or farin$2 or panwarfin$2 or prothromadin$2 or simarc$2 or sofarin$2 or tedicumar$2 or tintorane$2 or uniwarfin$2 or waran$2 or warfant$2 or warfar$2 or warfil$2 or warfilone$2 or warnerin$2).ti,ab,kf,rn,nm. (39538)

26 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI).ti,ab,kf,rn,nm. (17516)

27 Acenocoumarol/ (1252)

28 acenocoumarol$.ti,ab,kf,rn,nm. (1584)

29 (acenocoumarin$2 or acenocoumarine$2 or acenocoumarole$2 or acenocoumarolum$2 or acenocumarol$2 or acenocumarolo$2 or acenocumerol$2 or acenokumarin$2 or acitrom$2 or ascumar$2 or coumarin$2 or g 23 350 or g23 350 or g-2335 or g2335 or g-23350 or g23350 or minisintrom$2 or neosintrom$2 or neositron$2 or nicoumalone$2 or nicumalon$2 or niffcoumar$2 or nitrovarfarian$2 or nitrowarfarin$2 or sincoumar$2 or sincumar$2 or sinkumar$2 or sinthrom$2 or sinthrome$2 or sintroma$2 or sintron$2 or syncoumar$2 or syncumar$2 or synthrom$2 or syntrom$2 or trombostop$2 or zotil$2).ti,ab,kf,rn,nm. (18815)

30 (152-72-7 or 205-807-3 or I6WP63U32H).ti,ab,kf,rn,nm. (1252)

31 Phenindione/ (870)

32 phenindione$.ti,ab,kf,rn,nm. (895)

33 (acluton$2 or acoagine$2 or arthrombon$2 or athrombon$2 or bindan$2 or cronodione$2 or dandilone$2 or danilone$2 or diadilan$2 or dindevan$2 or dineval$2 or diophindane$2 or emandione$2 or eridione$2 or eridone$2 or fenhydren$2 or fenilin$2 or hedulin$2 or hemolidione$2 or indema$2 or indon$2 or nsc-41693 or phenidione$2 or phenindion$2 or phenyl indanedione$2 or phenylin$2 or phenylindandione$2 or phenylindane dion$2 or phenylindanedione$2 or phenyline$2 or phenyllin$2 or pindione$2 or rectadione$2 or thromasal$2 or thrombantin$2 or thrombasal$2 or thrombosan$2 or thrombusal$2 or trompid$2).ti,ab,kf,rn,nm. (943)

34 (83-12-5 or 5M7Y6274ZE or 201-454-4).ti,ab,kf,rn,nm. (870)

35 exp heparin/ (61526)

36 heparin$.ti,ab,kf,rn,nm. (98374)

37 (beparine$2 or clarin$2 or contusol$2 or disebrin$2 or eleparon$2 or elheparon$2 or epiheparin$2 or gag 98$2 or helberina$2 or hep flush kit$2 or hep lock$2 or hep-pak$2 or hepaflex$2 or hepalean$2 or heparitin$2 or hepcon$2 or hepflush$2 or hepsal$2 or inhepar$2 or inviclot$2 or lipo hepin$2 or lipohepin$ or liquaemin$2 or liquemin$2 or liquemine$2 or menaven$2 or monoparin$2 or mucoitin$2 or multiparin$2 or nevparin$2 or noparin$2 or panheparin$2 or panhepin$2 or panheprin$2 or parinix$2 or praecivenin$2 or pularin$2 or thrombareduct$ or thrombo vetren$2 or thromboliquin$2 or thromboliquine$2 or thrombophlogat$2 or thrombophob$2 or thromboreduct$ or thrombosamine$2 or uniparin$2 or vetren$2 or vister$).ti,ab,kf,rn,nm. (6433)

38 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A).ti,ab,kf,rn,nm. (52332)

39 (lmwh or lmwhs).ti,ab,kf,rn,nm. (4637)
40 (bm 2123 or bm2123 or choay$2 or ebpm$ or ff 1034 or ff1034 or fr 860 or fr860 or gag 869 or "pk 007" or sandoz 5100 or sandoz 6700 or traxyparine$2).ti,ab,kf,rn,nm. (112)
41 dalteparin$.ti,ab,kf,rn,nm. (1240)
42 (boxol$2 or fr-860 or fr860 or fragmin$2 or fragmine$2 or k 2165 or k2165 or kabi-2165 or kabi2165 or liquemin$2 or liquemine$2 or tedelparin$2).ti,ab,kf,rn,nm. (466)
43 (9041-08-1 or 12M44VTJ7B or S79O08V79F).ti,ab,kf,rn,nm. (836)
44 enoxaparin$.ti,ab,kf,rn,nm. (4811)
45 (clexan$2 or clexane$2 or emt-966 or emt-967 or emt966 or emt967 or inhixa$2 or klexane$2 or lovenox$2 or neoparin$2 or pk 10 169 or pk 10169 or pk10169 or pk10 169 or rp54563 or rp-54563 or thorinane$2).ti,ab,kf,rn,nm. (276)
46 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O).ti,ab,kf,rn,nm. (52332)
47 tinzaparin$.ti,ab,kf,rn,nm. (440)
48 (innohep$2 or lhn1 or lhn-1 or logiparin$2).ti,ab,kf,rn,nm. (67)
49 (9041-08-1 or 3S182ET3UA).ti,ab,kf,rn,nm. (1)
50 or/6-49 (161796)
51 meta-analysis as topic/ (15986)
52 meta-analysis.pt. (85010)
53 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kf. (239823)
54 or/51-53 (262502)
55 5 and 50 and 54 (499)
56 randomized controlled trial.pt. (454129)
57 (random$ or placebo).ti,ab,kf. (1031805)
58 or/56-57 (1128998)
59 5 and 50 and 58 (1694)
60 case-control studies/ (243410)
61 case-control$.ti,ab,kf. (109653)
62 (Epidemiologic Studies/ or Cohort Studies/ or follow-up studies/ or longitudinal studies/ or prospective studies/ or retrospective studies/ or Cross-Sectional Studies/ or observational study/ or Registries/) and comparative study/ (326843)
63 (Epidemiologic Studies/ or Cohort Studies/ or follow-up studies/ or longitudinal studies/ or prospective studies/ or retrospective studies/ or Cross-Sectional Studies/ or observational study/ or Registries/) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$).ti,ab,kf. (1057774)

64 (epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries).ti,ab,kf. and comparative study/ (136845)
65 ((epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$)).ti,ab,kf. (767388)
66 or/60-65 (1661429)
67 5 and 50 and 66 (2112)
68 patient compliance/ or medication adherence/ (66971)
69 (comply or complied or complying or noncomplying or complies or compliant or noncompliant or compliance or noncompliance or persist$ or nonpersist$ or concordan$ or nonconcordan$ or capacitan$ or noncapacitan$ or adhere or adhered or adhering or adheres or adherent or adherence or nonadher$).ti,ab,kf. (747892)
70 (Practice Patterns, Physicians'/ and (exp Prescriptions/ or Inappropriate Prescribing/)) or exp Prescriptions/sn, td or Inappropriate Prescribing/sn, td (10655)
71 ((prescription$1 or prescrib$) adj5 (pattern$1 or trend or trends or practice or practices or number$1 or statistic$ or data or datas or level or levels)).ti,ab,kf. (22347)
72 or/68-71 (800806)
73 5 and 50 and 72 (1150)
74 exp Great Britain/ (341295)
75 (national health service* or nhs*).ti,ab,in. (149469)
76 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (88169)
77 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in. (1786666)
78 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or

("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in. (1165735)

79 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in. (44877)

80 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in. (168580)

81 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in. (21083)

82 or/74-81 (2304822)

83 (exp africa/ or exp americas/ or exp antarctic regions/ or exp arctic regions/ or exp asia/ or exp australia/ or exp oceania/) not (exp great britain/ or europe/) (2544799)

84 82 not 83 (2183005)

85 exp United States/ (1251962)

86 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,jw,in,kf. (5935897)

87 exp Europe/ or European Union/ (1297291)

88 (europe$ or eu or "eu’s" or "e.u." or 5eu or eu5).ti,ab,kf,jw,in. (794818)

89 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kf,jw,in. (5084379)

90 exp Canada/ (142297)

91 (canada$ or canadian$).ti,ab,kf,jw,in. (848535)

92 australasia/ or exp australia/ (126204)

93 (australia$ or australas$).ti,ab,jw,kf,in. (599081)

94 New Zealand/ (35342)
95 new zealand$.ti,ab,jw,kf,in. (152885)
96 or/84-95 (14538443)
97 59 and 96 (1402)
98 67 and 96 (1718)
99 73 and 84 (145)
100 55 or 97 or 98 or 99 (2911)
101 exp animals/ not humans/ (4428087)
102 (news or editorial or case reports).pt. or case report.ti. (2554169)
103 100 not (101 or 102) (2872)
104 limit 103 to (english language and yr="2011 -Current") (1956)
105 remove duplicates from 104 (1946)

Source: Embase 1974 to 2018 February 28
Interface / URL: OvidSP
Database coverage dates: 1974 to 2018 February 28
Search date: 01/03/18
Retrieved records: 2789
Search strategy:

1 exp *atrial fibrillation/ (15984)
2 ((atrial or atrium or auricular or heart or cardiac) adj3 (fibrillat$ or tachycardia$ or tachyarrhythmia$)).ti,ab,kw. (110379)
3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib).ti,ab,kw. (72194)
4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib).ti,ab,kw. (1477)
5 or/1-4 (141312)
6 apixaban/ (7398)
7 apixaban$.ti,ab,kw,rn,tn. (7727)
8 (bms 562247 or bms562247 or eliques$2 or eliquis$2).ti,ab,kw,rn,tn. (502)
9 (503612-47-3 or 3Z9Y7UWC1J).ti,ab,kw,rn,tn. (6154)
10 dabigatran/ or dabigatran etexilate/ (11555)
11 (dabigatran$ or bibr 1048 or bibr1048 or pradaxa$2 or pradax$2 or prazaxa$2 or rendix$2).ti,ab,kw,rn,tn. (7781)
12 (211915-06-9 or I0VM4M70GC).ti,ab,kw,rn,tn. (0)
13 rivaroxaban/ (11359)
14 rivaroxaban$.ti,ab,kw,rn,tn. (11741)
15 (bay 59 7939 or bay 597939 or bay59 7939 or bay597939 or xarelto$2).ti,ab,kw,rn,tn. (1078)
16 (366789-02-8 or 9NDF7JZ4M3).ti,ab,kw,rn,tn. (9120)
17 edoxaban/ (2545)
18 edoxaban$.ti,ab,kw,rn,tn. (2714)

19 (du 176 or du 176b or du176 or du176b or lixiana$2 or savaysa$2 or endoxaban$2 or roteas$2).ti,ab,kw,rn,tn. (365)
20 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO).ti,ab,kw,rn,tn. (2265)
21 antivitamin K/ (11319)
22 ((vitamin k or vitamins k) adj3 (antagonist$1 or inhibitor$1 or blocker$1)).ti,ab,kw,rn,tn. (8034)
23 (anti vitamin k or antivitamin k or anti vitamins k or antivitamins k or menadione antagonist$1).ti,ab,kw,rn,tn. (670)
24 (vka or vkas).ti,ab,kw,rn,tn. (3274)
25 warfarin/ (81849)
26 warfarin$.ti,ab,kw,rn,tn. (84797)
27 (acetonylbenzylhydroxycoumarin$2 or adoisine$2 or aldocumar$2 or antrombin k$2 or athrombin$2 or athrombine$2 or athrombinek$2 or befarin$2 or carfin$2 or circuvit$2 or compound 42$2 or coumadan$ or coumadin$2 or coumadine$2 or coumafene$2 or coumaphene$2 or dagonal$2 or farin$2 or hydroxycoumarin$2 or jantoven$2 or kumatox$2 or maforan$2 or marevan$2 or farin$2 or panwarfin$2 or prothromadin$2 or simarc$2 or sofarin$2 or tedicumar$2 or tintorane$2 or uniwarfin$2 or waran$2 or warfant$2 or warfar$2 or warfil$2 or warfilone$2 or warnerin$2).ti,ab,kw,rn,tn. (95687)
28 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI).ti,ab,kw,rn,tn. (72548)
29 acenocoumarol/ (5694)
30 acenocoumarol$.ti,ab,kw,rn,tn. (5706)
31 (acenocoumarin$2 or acenocoumarine$2 or acenocoumarole$2 or acenocoumarolum$2 or acenocumarol$2 or acenocumarolo$2 or acenocumerol$2 or acenokumarin$2 or acitrom$2 or ascumar$2 or coumarin$2 or g 23 350 or g23 350 or g-2335 or g2335 or g-23350 or g23350 or minisintrom$2 or neosintrom$2 or neositron$2 or nicoumalone$2 or nicumalon$2 or niffcoumar$2 or nitrovarfarian$2 or nitrowarfarin$2 or sincoumar$2 or sincumar$2 or sinkumar$2 or sinthrom$2 or sinthrome$2 or sintroma$2 or sintron$2 or syncoumar$2 or syncumar$2 or synthrom$2 or syntrom$2 or trombostop$2 or zotil$2).ti,ab,kw,rn,tn. (19150)
32 (152-72-7 or 205-807-3 or I6WP63U32H).ti,ab,kw,rn,tn. (5322)
33 phenindione/ (1264)
34 phenindione$.ti,ab,kw,rn,tn. (1276)
35 (acluton$2 or acoagine$2 or arthrombon$2 or athrombon$2 or bindan$2 or cronodione$2 or dandilone$2 or danilone$2 or diadilan$2 or dindevan$2 or dineval$2 or diophindane$2 or emandione$2 or eridione$2 or eridone$2 or fenhydren$2 or fenilin$2 or hedulin$2 or hemolidione$2 or indema$2 or indon$2 or nsc-41693 or phenidione$2 or phenindion$2 or phenyl indanedione$2 or phenylin$2 or phenylindandione$2 or phenylindane dion$2 or phenylindanedione$2 or phenyline$2 or phenyllin$2 or pindione$2 or rectadione$2 or thromasal$2 or thrombantin$2 or thrombasal$2 or thrombosan$2 or thrombusal$2 or trompid$2).ti,ab,kw,rn,tn. (1327)

36 (83-12-5 or 5M7Y6274ZE or 201-454-4).ti,ab,kw,rn,tn. (1259)
37 heparin/ (136947)
38 heparin derivative/ or heparinoid/ or low molecular weight heparin/ (36472)
39 heparin$.ti,ab,kw,rn,tn. (179355)
40 (beparine$2 or clarin$2 or contusol$2 or disebrin$2 or eleparon$2 or elheparon$2 or epiheparin$2 or gag 98$2 or helberina$2 or hep flush kit$2 or hep lock$2 or hep-pak$2 or hepaflex$2 or hepalean$2 or heparitin$2 or hepcon$2 or hepflush$2 or hepsal$2 or inhepar$2 or inviclot$2 or lipo hepin$2 or lipohepin$ or liquaemin$2 or liquemin$2 or liquemine$2 or menaven$2 or monoparin$2 or mucoitin$2 or multiparin$2 or nevparin$2 or noparin$2 or panheparin$2 or panhepin$2 or panheprin$2 or parinix$2 or praecivenin$2 or pularin$2 or thrombareduct$ or thrombo vetren$2 or thromboliquin$2 or thromboliquine$2 or thrombophlogat$2 or thrombophob$2 or thromboreduct$ or thrombosamine$2 or uniparin$2 or vetren$2 or vister$).ti,ab,kw,rn,tn. (1879)
41 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A).ti,ab,kw,rn,tn. (125878)
42 (lmwh or lmwhs).ti,ab,kw,rn,tn. (8490)
43 (bm 2123 or bm2123 or choay$2 or ebpm$ or ff 1034 or ff1034 or fr 860 or fr860 or gag 869 or "pk 007" or sandoz 5100 or sandoz 6700 or traxyparine$2).ti,ab,kw,rn,tn. (395)
44 dalteparin/ (7173)
45 dalteparin$.ti,ab,kw,rn,tn. (1553)
46 (boxol$2 or fr-860 or fr860 or fragmin$2 or fragmine$2 or k 2165 or k2165 or kabi-2165 or kabi2165 or liquemin$2 or liquemine$2 or tedelparin$2).ti,ab,kw,rn,tn. (2807)
47 (9041-08-1 or 12M44VTJ7B or S79O08V79F).ti,ab,kw,rn,tn. (8403)
48 enoxaparin/ (21417)
49 enoxaparin$.ti,ab,kw,rn,tn. (21681)
50 (clexan$2 or clexane$2 or emt-966 or emt-967 or emt966 or emt967 or inhixa$2 or klexane$2 or lovenox$2 or neoparin$2 or pk 10 169 or pk 10169 or pk10169 or pk10 169 or rp54563 or rp-54563 or thorinane$2).ti,ab,kw,rn,tn. (3203)
51 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O).ti,ab,kw,rn,tn. (10907)
52 tinzaparin/ (2956)
53 tinzaparin$.ti,ab,kw,rn,tn. (711)
54 (innohep$2 or lhn1 or lhn-1 or logiparin$2).ti,ab,kw,rn,tn. (701)
55 (9041-08-1 or 3S182ET3UA).ti,ab,kw,rn,tn. (8403)
56 or/6-55 (298522)
57 "systematic review"/ or "systematic review (topic)"/ (177962)
58 meta analysis/ or "meta analysis (topic)"/ (172241)
59 (systematic$ review$ or meta-analytic$ or metanalysis or metaanalysis or meta-analysis or meta-synthesis or metasynthesis or meta-regression or metaregression or integrative review or data synthesis or research synthesis or narrative synthesis or systematic study or systematic studies or systematic comparison$ or systematic overview$ or evidence based review or comprehensive review or critical review or

quantitative review or structured review or realist review or realist synthesis or (synthes$ adj3 (literature or evidence))).ti,ab,kw. (297074)
60 or/57-59 (393960)
61 5 and 56 and 60 (1398)
62 Randomized controlled trial/ (489138)
63 randomization/ (77116)
64 (random$ or placebo).ti,ab,kw. (1373217)
65 or/62-64 (1478748)
66 5 and 56 and 65 (3300)
67 exp case control study/ (139831)
68 case-control$.ti,ab,kw. (140624)
69 (Clinical study/ or Family study/ or Longitudinal study/ or Retrospective study/ or Prospective study/ or Cohort analysis/ or observational study/ or register/) and exp comparative study/ (141771)
70 (Clinical study/ or Family study/ or Longitudinal study/ or Retrospective study/ or Prospective study/ or Cohort analysis/ or observational study/ or register/) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$).ti,ab,kw. (952461)
71 (epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries).ti,ab,kw. and exp comparative study/ (102339)
72 ((epidemiolog$ study or epidemiolog$ studies or cohort or cohorts or follow-up study or follow-up studies or longitudinal study or longitudinal studies or prospective study or prospective studies or retrospective study or retrospective studies or cross-sectional or observational or register or registers or registry or registries) and (group$ or control or controls or controlled or versus or compare or compares or compared or comparing or comparison or comparisons or comparative or assign$ or match or matched or matching or allocat$)).ti,ab,kw. (1176961)
73 or/67-72 (1737995)
74 5 and 56 and 73 (4306)
75 patient compliance/ or medication compliance/ (134114)
76 (comply or complied or complying or noncomplying or complies or compliant or noncompliant or compliance or noncompliance or persist$ or nonpersist$ or concordan$ or nonconcordan$ or capacitan$ or noncapacitan$ or adhere or adhered or adhering or adheres or adherent or adherence or nonadher$).ti,ab,kw. (1019664)
77 clinical practice/ and (prescription/ or electronic prescribing/ or exp inappropriate prescribing/) (11138)
78 (prescription/ or electronic prescribing/ or exp inappropriate prescribing/) and statistics/ (3687)

79 ((prescription$1 or prescrib$) adj5 (pattern$1 or trend or trends or practice or practices or number$1 or statistic$ or data or datas or level or levels)).ti,ab,kw. (37318)
80 or/75-79 (1116514)
81 5 and 56 and 80 (3500)
82 United Kingdom/ (387877)
83 (national health service* or nhs*).ti,ab,in,ad. (274175)
84 (english not ((published or publication* or translat* or written or language* or speak* or literature or citation*) adj5 english)).ti,ab. (34301)
85 (gb or "g.b." or britain* or (british* not "british columbia") or uk or "u.k." or united kingdom* or (england* not "new england") or northern ireland* or northern irish* or scotland* or scottish* or ((wales or "south wales") not "new south wales") or welsh*).ti,ab,jw,in,ad. (2843490)
86 (bath or "bath's" or ((birmingham not alabama*) or ("birmingham's" not alabama*) or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or carlisle* or "carlisle's" or (cambridge not (massachusetts* or boston* or harvard*)) or ("cambridge's" not (massachusetts* or boston* or harvard*)) or (canterbury not zealand*) or ("canterbury's" not zealand*) or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or derby or "derby's" or (durham not (carolina* or nc)) or ("durham's" not (carolina* or nc)) or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds* or leicester or "leicester's" or (lincoln not nebraska*) or ("lincoln's" not nebraska*) or (liverpool not (new south wales* or nsw)) or ("liverpool's" not (new south wales* or nsw)) or ((london not (ontario* or ont or toronto*)) or ("london's" not (ontario* or ont or toronto*)) or manchester or "manchester's" or (newcastle not (new south wales* or nsw)) or ("newcastle's" not (new south wales* or nsw)) or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's" or (worcester not (massachusetts* or boston* or harvard*)) or ("worcester's" not (massachusetts* or boston* or harvard*)) or (york not ("new york*" or ny or ontario* or ont or toronto*)) or ("york's" not ("new york*" or ny or ontario* or ont or toronto*))))).ti,ab,in,ad. (2120402)
87 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st davids or swansea or "swansea's").ti,ab,in,ad. (85626)
88 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or "glasgow's" or inverness or (perth not australia*) or ("perth's" not australia*) or stirling or "stirling's").ti,ab,in,ad. (293907)
89 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or derry or "derry's" or newry or "newry's").ti,ab,in,ad. (38586)

90 or/82-89 (3467297)
91 (exp "arctic and antarctic"/ or exp oceanic regions/ or exp western hemisphere/ or exp africa/ or exp asia/ or exp "australia and new zealand"/) not (united kingdom/ or europe/) (2770488)
92 90 not 91 (3289294)
93 exp United States/ (1161790)
94 (america$ or united states or US or "U.S." or USA or "U.S.A.").ti,ab,kw,jw,ad. (9262416)
95 exp Europe/ or european union/ (1491672)
96 (europe$ or eu or "eu's" or "e.u." or 5eu or eu5).ti,ab,kw,jw,ad. (1232827)
97 (austria$ or belgium$ or belgian$ or bulgaria$ or croat$ or cyprus$ or cypriot$ or czech$ or denmark$ or danish$ or estonia$ or finland$ or finnish or finns or france$ or french$ or german$ or greece$ or greek$ or hungar$ or iceland$ or ireland$ or irish$ or italy$ or italian$ or latvia$ or lithuania$ or luxembourg$ or malta$ or maltese$ or netherland$ or dutch$ or holland$ or norway$ or norwegian$ or poland$ or polish$ or portugal$ or portugues$ or romania$ or slovak$ or slovenia$ or spain$ or spanish$ or swede$ or swedish$ or switzerland$ or swiss$ or turkey$ or turkish$ or turks).ti,ab,kw,jw,ad. (8006300)
98 exp Canada/ (163495)
99 (canada$ or canadian$).ti,ab,kw,jw,ad. (981812)
100 exp "Australia and New Zealand"/ (199567)
101 (australia$ or australas$).ti,ab,kw,jw,ad. (710895)
102 new zealand$.ti,ab,kw,jw,ad. (174191)
103 or/93-102 (19536502)
104 92 or 103 (21274306)
105 66 and 104 (2917)
106 74 and 104 (3681)
107 81 and 92 (605)
108 61 or 105 or 106 or 107 (6848)
109 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5808034)
110 editorial.pt. or case report.ti. (813263)
111 conference abstract.pt. (2898647)
112 108 not (109 or 110 or 111) (4456)
113 limit 112 to (english language and yr="2011 -Current") (2879)
114 remove duplicates from 113 (2789)

Source: Cochrane Database of Systematic Reviews: Issue 2 of 12, February 2018
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 01/03/18
Retrieved records: 9

Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3591
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)):ti,ab,kw 9828
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib):ti,ab,kw 4623
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib):ti,ab,kw 131
#5 #1 or #2 or #3 or #4 10911
#6 apixaban*:ti,ab,kw 532
#7 ("bms 562247" or bms562247 or eliques* or eliquis*) 15
#8 (503612-47-3 or 3Z9Y7UWC1J):ti,ab,kw 0
#9 [mh ^Dabigatran] 132
#10 (dabigatran* or "bibr 1048" or bibr1048 or pradaxa* or pradax* or prazaxa* or rendix*):ti,ab,kw 688
#11 (211915-06-9 or I0VM4M70GC):ti,ab,kw 0
#12 [mh ^Rivaroxaban] 197
#13 rivaroxaban*:ti,ab,kw 867
#14 ("bay 59 7939" or "bay 597939" or "bay59 7939" or bay597939 or xarelto*):ti,ab,kw 36
#15 (366789-02-8 or 9NDF7JZ4M3):ti,ab,kw 0
#16 edoxaban*:ti,ab,kw 300
#17 ("du 176" or "du 176b" or du176 or du176b or lixiana* or savaysa* or endoxaban* or roteas*):ti,ab,kw 13
#18 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO):ti,ab,kw 0
#19 [mh "Vitamin K"/ai] 160
#20 (("vitamin k" or "vitamins k") near/3 (antagonist* or inhibitor* or blocker*)):ti,ab,kw 632
#21 ("anti vitamin k" or "antivitamin k" or "anti vitamins k" or "antivitamins k" or menadione next antagonist*):ti,ab,kw 431
#22 (vka or vkas):ti,ab,kw 281
#23 [mh ^Warfarin] 1504
#24 warfarin*:ti,ab,kw 3743
#25 (acetonylbenzylhydroxycoumarin* or adoisine* or aldocumar* or antrombin next k* or athrombin* or athrombine* or athrombinek* or befarin* or carfin* or circuvit* or compound next 42* or coumadan* or coumadin* or coumadine* or coumafene* or coumaphene* or dagonal* or farin* or hydroxycoumarin* or jantoven* or kumatox* or maforan* or marevan* or farin* or panwarfin* or prothromadin* or simarc* or sofarin* or tedicumar* or tintorane* or uniwarfin* or waran* or warfant* or warfar* or warfil* or warfilone* or warnerin*):ti,ab,kw 4217
#26 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI):ti,ab,kw 6

#27 [mh ^Acenocoumarol] 118
#28 acenocoumarol*:ti,ab,kw 246
#29 (acenocoumarin* or acenocoumarine* or acenocoumarole* or acenocoumarolum* or acenocumarol* or acenocumarolo* or acenocumerol* or acenokumarin* or acitrom* or ascumar* or coumarin* or "g 23 350" or "g23 350" or g-2335 or g2335 or g-23350 or g23350 or minisintrom* or neosintrom* or neositron* or nicoumalone* or nicumalon* or niffcoumar* or nitrovarfarian* or nitrowarfarin* or sincoumar* or sincumar* or sinkumar* or sinthrom* or sinthrome* or sintroma* or sintron* or syncoumar* or syncumar* or synthrom* or syntrom* or trombostop* or zotil*):ti,ab,kw 333
#30 (152-72-7 or 205-807-3 or I6WP63U32H):ti,ab,kw 0
#31 [mh ^Phenindione] 27
#32 phenindione*:ti,ab,kw 35
#33 (acluton* or acoagine* or arthrombon* or athrombon* or bindan* or cronodione* or dandilone* or danilone* or diadilan* or dindevan* or dineval* or diophindane* or emandione* or eridione* or eridone* or fenhydren* or fenilin* or hedulin* or hemolidione* or indema* or indon or indonr or indontm or nsc-41693 or phenidione* or phenindion* or phenyl next indanedione* or phenylin* or phenylindandione* or phenylindane next dion* or phenylindanedione* or phenyline* or phenyllin* or pindione* or rectadione* or thromasal* or thrombantin* or thrombasal* or thrombosan* or thrombusal* or trompid*):ti,ab,kw 59
#34 (83-12-5 or 5M7Y6274ZE or 201-454-4):ti,ab,kw 0
#35 [mh heparin] 4519
#36 heparin*:ti,ab,kw 10238
#37 (beparine* or clarin* or contusol* or disebrin* or eleparon* or elheparon* or epiheparin* or gag next 98* or helberina* or hep next flush next kit* or hep next lock* or hep-pak* or hepaflex* or hepalean* or heparitin* or hepcon* or hepflush* or hepsal* or inhepar* or inviclot* or lipo next hepin* or lipohepin* or liquaemin* or liquemin* or liquemine* or menaven* or monoparin* or mucoitin* or multiparin* or nevparin* or noparin* or panheparin* or panhepin* or panheprin* or parinix* or praecivenin* or pularin* or thrombareduct* or thrombo next vetren* or thromboliquin* or thromboliquine* or thrombophlogat* or thrombophob* or thromboreduct* or thrombosamine* or uniparin* or vetren* or vister*):ti,ab,kw 171
#38 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A):ti,ab,kw 0
#39 (lmwh or lmwhs):ti,ab,kw 1009
#40 ("bm 2123" or bm2123 or choay* or ebpm* or "ff 1034" or ff1034 or "fr 860" or fr860 or "gag 869" or "pk 007" or "sandoz 5100" or "sandoz 6700" or traxyparine*):ti,ab,kw 19
#41 dalteparin*:ti,ab,kw 516
#42 (boxol* or fr-860 or fr860 or fragmin* or fragmine* or "k 2165" or k2165 or kabi-2165 or kabi2165 or liquemin* or liquemine* or tedelparin*):ti,ab,kw 231
#43 (9041-08-1 or 12M44VTJ7B or S79O08V79F):ti,ab,kw 0

#44 enoxaparin*:ti,ab,kw 1708
#45 (clexan* or clexane* or emt-966 or emt-967 or emt966 or emt967 or inhixa* or klexane* or lovenox* or neoparin* or "pk 10 169" or "pk 10169" or pk10169 or "pk10 169" or rp54563 or rp-54563 or thorinane*):ti,ab,kw 59
#46 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O):ti,ab,kw 0
#47 tinzaparin*:ti,ab,kw 183
#48 (innohep* or lhn1 or lhn-1 or logiparin*):ti,ab,kw 41
#49 (9041-08-1 or 3S182ET3UA):ti,ab,kw 0
#50 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 16028
#51 #5 and #50 1918
#52 #51 Publication Year from 2011 to 2018 1369
#53 #52 in Cochrane Reviews (Reviews and Protocols) 9

Source: Database of Abstracts of Reviews of Effects: Issue 2 of 4, April 2015
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 01/03/18
Retrieved records: 44
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3591
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10383
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11058
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 135
#5 #1 or #2 or #3 or #4 17707
#6 apixaban* 577
#7 ("bms 562247" or bms562247 or eliques* or eliquis*) 15
#8 (503612-47-3 or 3Z9Y7UWC1J) 0
#9 [mh ^Dabigatran] 132
#10 (dabigatran* or "bibr 1048" or bibr1048 or pradaxa* or pradax* or prazaxa* or rendix*) 744
#11 (211915-06-9 or I0VM4M70GC) 0
#12 [mh ^Rivaroxaban] 197
#13 rivaroxaban* 925
#14 ("bay 59 7939" or "bay 597939" or "bay59 7939" or bay597939 or xarelto*) 56
#15 (366789-02-8 or 9NDF7JZ4M3) 0
#16 edoxaban* 324

#17 ("du 176" or "du 176b" or du176 or du176b or lixiana* or savaysa* or endoxaban* or roteas*) 41
#18 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO) 0
#19 [mh "Vitamin K"/ai] 160
#20 (("vitamin k" or "vitamins k") near/3 (antagonist* or inhibitor* or blocker*)) 779
#21 ("anti vitamin k" or "antivitamin k" or "anti vitamins k" or "antivitamins k" or menadione next antagonist*) 449
#22 (vka or vkas) 330
#23 [mh ^Warfarin] 1504
#24 warfarin* 4231
#25 (acetonylbenzylhydroxycoumarin* or adoisine* or aldocumar* or antrombin next k* or athrombin* or athrombine* or athrombinek* or befarin* or carfin* or circuvit* or compound next 42* or coumadan* or coumadin* or coumadine* or coumafene* or coumaphene* or dagonal* or farin* or hydroxycoumarin* or jantoven* or kumatox* or maforan* or marevan* or farin* or panwarfin* or prothromadin* or simarc* or sofarin* or tedicumar* or tintorane* or uniwarfin* or waran* or warfant* or warfar* or warfil* or warfilone* or warnerin*) 5507
#26 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI) 6
#27 [mh ^Acenocoumarol] 118
#28 acenocoumarol* 311
#29 (acenocoumarin* or acenocoumarine* or acenocoumarole* or acenocoumarolum* or acenocumarol* or acenocumarolo* or acenocumerol* or acenokumarin* or acitrom* or ascumar* or coumarin* or "g 23 350" or "g23 350" or g-2335 or g2335 or g-23350 or g23350 or minisintrom* or neosintrom* or neositron* or nicoumalone* or nicumalon* or niffcoumar* or nitrovarfarian* or nitrowarfarin* or sincoumar* or sincumar* or sinkumar* or sinthrom* or sinthrome* or sintroma* or sintron* or syncoumar* or syncumar* or synthrom* or syntrom* or trombostop* or zotil*) 437
#30 (152-72-7 or 205-807-3 or I6WP63U32H) 0
#31 [mh ^Phenindione] 27
#32 phenindione* 64
#33 (acluton* or acoagine* or arthrombon* or athrombon* or bindan* or cronodione* or dandilone* or danilone* or diadilan* or dindevan* or dineval* or diophindane* or emandione* or eridione* or eridone* or fenhydren* or fenilin* or hedulin* or hemolidione* or indema* or indon or indonr or indontm or nsc-41693 or phenidione* or phenindion* or phenyl next indanedione* or phenylin* or phenylindandione* or phenylindane next dion* or phenylindanedione* or phenyline* or phenyllin* or pindione* or rectadione* or thromasal* or thrombantin* or thrombasal* or thrombosan* or thrombusal* or trompid*) 91
#34 (83-12-5 or 5M7Y6274ZE or 201-454-4) 1
#35 [mh heparin] 4519
#36 heparin* 10868

#37 (beparine* or clarin* or contusol* or disebrin* or eleparon* or elheparon* or epiheparin* or gag next 98* or helberina* or hep next flush next kit* or hep next lock* or hep-pak* or hepaflex* or hepalean* or heparitin* or hepcon* or hepflush* or hepsal* or inhepar* or inviclot* or lipo next hepin* or lipohepin* or liquaemin* or liquemin* or liquemine* or menaven* or monoparin* or mucoitin* or multiparin* or nevparin* or noparin* or panheparin* or panhepin* or panheprin* or parinix* or praecivenin* or pularin* or thrombareduct* or thrombo next vetren* or thromboliquin* or thromboliquine* or thrombophlogat* or thrombophob* or thromboreduct* or thrombosamine* or uniparin* or vetren* or vister*) 210
#38 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A) 2
#39 (lmwh or lmwhs) 1245
#40 ("bm 2123" or bm2123 or choay* or ebpm* or "ff 1034" or ff1034 or "fr 860" or fr860 or "gag 869" or "pk 007" or "sandoz 5100" or "sandoz 6700" or traxyparine*) 42
#41 dalteparin* 649
#42 (boxol* or fr-860 or fr860 or fragmin* or fragmine* or "k 2165" or k2165 or kabi-2165 or kabi2165 or liquemin* or liquemine* or tedelparin*) 307
#43 (9041-08-1 or 12M44VTJ7B or S79O08V79F) 1
#44 enoxaparin* 1914
#45 (clexan* or clexane* or emt-966 or emt-967 or emt966 or emt967 or inhixa* or klexane* or lovenox* or neoparin* or "pk 10 169" or "pk 10169" or pk10169 or "pk10 169" or rp54563 or rp-54563 or thorinane*) 114
#46 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O) 1
#47 tinzaparin* 271
#48 (innohep* or lhn1 or lhn-1 or logiparin*) 89
#49 (9041-08-1 or 3S182ET3UA) 1
#50 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 17727
#51 #5 and #50 2289
#52 #51 Publication Year from 2011 to 2018 1575
#53 #52 in Other Reviews 44
#54 #52 in Technology Assessments 16

Source: Health Technology Assessment Database: Issue 4 of 4, October 2016
Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 01/03/18
Retrieved records: 16
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3591

#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10383
#3 (AF or A-Fib or AFib or PAF or PA-Fib or PAFib) 11058
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 135
#5 #1 or #2 or #3 or #4 17707
#6 apixaban* 577
#7 ("bms 562247" or bms562247 or eliques* or eliquis*) 15
#8 (503612-47-3 or 3Z9Y7UWC1J) 0
#9 [mh ^Dabigatran] 132
#10 (dabigatran* or "bibr 1048" or bibr1048 or pradaxa* or pradax* or prazaxa* or rendix*) 744
#11 (211915-06-9 or I0VM4M70GC) 0
#12 [mh ^Rivaroxaban] 197
#13 rivaroxaban* 925
#14 ("bay 59 7939" or "bay 597939" or "bay59 7939" or bay597939 or xarelto*) 56
#15 (366789-02-8 or 9NDF7JZ4M3) 0
#16 edoxaban* 324
#17 ("du 176" or "du 176b" or du176 or du176b or lixiana* or savaysa* or endoxaban* or roteas*) 41
#18 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO) 0
#19 [mh "Vitamin K"/ai] 160
#20 (("vitamin k" or "vitamins k") near/3 (antagonist* or inhibitor* or blocker*)) 779
#21 ("anti vitamin k" or "antivitamin k" or "anti vitamins k" or "antivitamins k" or menadione next antagonist*) 449
#22 (vka or vkas) 330
#23 [mh ^Warfarin] 1504
#24 warfarin* 4231
#25 (acetonylbenzylhydroxycoumarin* or adoisine* or aldocumar* or antrombin next k* or athrombin* or athrombine* or athrombinek* or befarin* or carfin* or circuvit* or compound next 42* or coumadan* or coumadin* or coumadine* or coumafene* or coumaphene* or dagonal* or farin* or hydroxycoumarin* or jantoven* or kumatox* or maforan* or marevan* or farin* or panwarfin* or prothromadin* or simarc* or sofarin* or tedicumar* or tintorane* or uniwarfin* or waran* or warfant* or warfar* or warfil* or warfilone* or warnerin*) 5507
#26 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI) 6
#27 [mh ^Acenocoumarol] 118
#28 acenocoumarol* 311
#29 (acenocoumarin* or acenocoumarine* or acenocoumarole* or acenocoumarolum* or acenocumarol* or acenocumarolo* or acenocumerol* or acenokumarin* or acitrom* or ascumar* or coumarin* or "g 23 350" or "g23 350" or g-2335 or g2335 or g-23350 or

g23350 or minisintrom* or neosintrom* or neositron* or nicoumalone* or nicumalon* or niffcoumar* or nitrovarfarian* or nitrowarfarin* or sincoumar* or sincumar* or sinkumar* or sinthrom* or sinthrome* or sintroma* or sintron* or syncoumar* or syncumar* or synthrom* or syntrom* or trombostop* or zotil*) 437
#30 (152-72-7 or 205-807-3 or I6WP63U32H) 0
#31 [mh ^Phenindione] 27
#32 phenindione* 64
#33 (acluton* or acoagine* or arthrombon* or athrombon* or bindan* or cronodione* or dandilone* or danilone* or diadilan* or dindevan* or dineval* or diophindane* or emandione* or eridione* or eridone* or fenhydren* or fenilin* or hedulin* or hemolidione* or indema* or indon or indonr or indontm or nsc-41693 or phenidione* or phenindion* or phenyl next indanedione* or phenylin* or phenylindandione* or phenylindane next dion* or phenylindanedione* or phenyline* or phenyllin* or pindione* or rectadione* or thromasal* or thrombantin* or thrombasal* or thrombosan* or thrombusal* or trompid*) 91
#34 (83-12-5 or 5M7Y6274ZE or 201-454-4) 1
#35 [mh heparin] 4519
#36 heparin* 10868
#37 (beparine* or clarin* or contusol* or disebrin* or eleparon* or elheparon* or epiheparin* or gag next 98* or helberina* or hep next flush next kit* or hep next lock* or hep-pak* or hepaflex* or hepalean* or heparitin* or hepcon* or hepflush* or hepsal* or inhepar* or inviclot* or lipo next hepin* or lipohepin* or liquaemin* or liquemin* or liquemine* or menaven* or monoparin* or mucoitin* or multiparin* or nevparin* or noparin* or panheparin* or panhepin* or panheprin* or parinix* or praecivenin* or pularin* or thrombareduct* or thrombo next vetren* or thromboliquin* or thromboliquine* or thrombophlogat* or thrombophob* or thromboreduct* or thrombosamine* or uniparin* or vetren* or vister*) 210
#38 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A) 2
#39 (lmwh or lmwhs) 1245
#40 ("bm 2123" or bm2123 or choay* or ebpm* or "ff 1034" or ff1034 or "fr 860" or fr860 or "gag 869" or "pk 007" or "sandoz 5100" or "sandoz 6700" or traxyparine*) 42
#41 dalteparin* 649
#42 (boxol* or fr-860 or fr860 or fragmin* or fragmine* or "k 2165" or k2165 or kabi-2165 or kabi2165 or liquemin* or liquemine* or tedelparin*) 307
#43 (9041-08-1 or 12M44VTJ7B or S79O08V79F) 1
#44 enoxaparin* 1914
#45 (clexan* or clexane* or emt-966 or emt-967 or emt966 or emt967 or inhixa* or klexane* or lovenox* or neoparin* or "pk 10 169" or "pk 10169" or pk10169 or "pk10 169" or rp54563 or rp-54563 or thorinane*) 114
#46 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O) 1
#47 tinzaparin* 271
#48 (innohep* or lhn1 or lhn-1 or logiparin*) 89

#49 (9041-08-1 or 3S182ET3UA) 1
#50 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 17727
#51 #5 and #50 2289
#52 #51 Publication Year from 2011 to 2018 1575
#53 #52 in Other Reviews 44
#54 #52 in Technology Assessments 16

Source: Cochrane Central Register of Controlled Trials: Issue 2 of 12, February 2018

Interface / URL: Cochrane Library / Wiley
Database coverage dates: Not given
Search date: 01/03/18
Retrieved records: 1256
Search strategy:

#1 [mh ^"Atrial Fibrillation"] 3591
#2 ((atrial or atrium or auricular or heart or cardiac) near/3 (fibrillat* or tachycardia* or tachyarrhythmia*)) 10383
#3 (A-Fib or AFib or PAF or PA-Fib or PAFib) or AF:ti,ab,kw 4665
#4 (NVAF or NVA-Fib or NVAFib or NVPAF or NVPA-Fib or NVPAFib) 135
#5 #1 or #2 or #3 or #4 11497
#6 apixaban* 577
#7 ("bms 562247" or bms562247 or eliques* or eliquis*) 15
#8 (503612-47-3 or 3Z9Y7UWC1J) 0
#9 [mh ^Dabigatran] 132
#10 (dabigatran* or "bibr 1048" or bibr1048 or pradaxa* or pradax* or prazaxa* or rendix*) 744
#11 (211915-06-9 or I0VM4M70GC) 0
#12 [mh ^Rivaroxaban] 197
#13 rivaroxaban* 925
#14 ("bay 59 7939" or "bay 597939" or "bay59 7939" or bay597939 or xarelto*) 56
#15 (366789-02-8 or 9NDF7JZ4M3) 0
#16 edoxaban* 324
#17 ("du 176" or "du 176b" or du176 or du176b or lixiana* or savaysa* or endoxaban* or roteas*) 41
#18 (480449-70-5 or 480449-71-6 or 912273-65-5 or NDU3J18APO) 0
#19 [mh "Vitamin K"/ai] 160
#20 (("vitamin k" or "vitamins k") near/3 (antagonist* or inhibitor* or blocker*)) 779

#21 ("anti vitamin k" or "antivitamin k" or "anti vitamins k" or "antivitamins k" or menadione next antagonist*) 449
#22 (vka or vkas) 330
#23 [mh ^Warfarin] 1504
#24 warfarin* 4231
#25 (acetonylbenzylhydroxycoumarin* or adoisine* or aldocumar* or antrombin next k* or athrombin* or athrombine* or athrombinek* or befarin* or carfin* or circuvit* or compound next 42* or coumadan* or coumadin* or coumadine* or coumafene* or coumaphene* or dagonal* or farin* or hydroxycoumarin* or jantoven* or kumatox* or maforan* or marevan* or farin* or panwarfin* or prothromadin* or simarc* or sofarin* or tedicumar* or tintorane* or uniwarfin* or waran* or warfant* or warfar* or warfil* or warfilone* or warnerin*) 5507
#26 (129-06-6 or 2610-86-8 or 3324-63-8 or 5543-58-8 or 81-81-2 or 5543-56-6 or 56573-89-8 or 5Q7ZVV76EI) 6
#27 [mh ^Acenocoumarol] 118
#28 acenocoumarol* 311
#29 (acenocoumarin* or acenocoumarine* or acenocoumarole* or acenocoumarolum* or acenocumarol* or acenocumarolo* or acenocumerol* or acenokumarin* or acitrom* or ascumar* or coumarin* or "g 23 350" or "g23 350" or g-2335 or g2335 or g-23350 or g23350 or minisintrom* or neosintrom* or neositron* or nicoumalone* or nicumalon* or niffcoumar* or nitrovarfarian* or nitrowarfarin* or sincoumar* or sincumar* or sinkumar* or sinthrom* or sinthrome* or sintroma* or sintron* or syncoumar* or syncumar* or synthrom* or syntrom* or trombostop* or zotil*) 437
#30 (152-72-7 or 205-807-3 or I6WP63U32H) 0
#31 [mh ^Phenindione] 27
#32 phenindione* 64
#33 (acluton* or acoagine* or arthrombon* or athrombon* or bindan* or cronodione* or dandilone* or danilone* or diadilan* or dindevan* or dineval* or diophindane* or emandione* or eridione* or eridone* or fenhydren* or fenilin* or hedulin* or hemolidione* or indema* or indon or indonr or indontm or nsc-41693 or phenidione* or phenindion* or phenyl next indanedione* or phenylin* or phenylindandione* or phenylindane next dion* or phenylindanedione* or phenyline* or phenyllin* or pindione* or rectadione* or thromasal* or thrombantin* or thrombasal* or thrombosan* or thrombusal* or trompid*) 91
#34 (83-12-5 or 5M7Y6274ZE or 201-454-4) 1
#35 [mh heparin] 4519
#36 heparin* 10868
#37 (beparine* or clarin* or contusol* or disebrin* or eleparon* or elheparon* or epiheparin* or gag next 98* or helberina* or hep next flush next kit* or hep next lock* or hep-pak* or hepaflex* or hepalean* or heparitin* or hepcon* or hepflush* or hepsal* or inhepar* or inviclot* or lipo next hepin* or lipohepin* or liquaemin* or liquemin* or liquemine* or menaven* or monoparin* or mucoitin* or multiparin* or nevparin* or noparin*

or panheparin* or panhepin* or panheprin* or parinix* or praecivenin* or pularin* or thrombareduct* or thrombo next vetren* or thromboliquin* or thromboliquine* or thrombophlogat* or thrombophob* or thromboreduct* or thrombosamine* or uniparin* or vetren* or vister*) 210
#38 (9005-49-6 or 37187-54-5 or 8057-48-5 or 8065-01-8 or T2410KM04A) 2
#39 (lmwh or lmwhs) 1245
#40 ("bm 2123" or bm2123 or choay* or ebpm* or "ff 1034" or ff1034 or "fr 860" or fr860 or "gag 869" or "pk 007" or "sandoz 5100" or "sandoz 6700" or traxyparine*) 42
#41 dalteparin* 649
#42 (boxol* or fr-860 or fr860 or fragmin* or fragmine* or "k 2165" or k2165 or kabi-2165 or kabi2165 or liquemin* or liquemine* or tedelparin*) 307
#43 (9041-08-1 or 12M44VTJ7B or S79O08V79F) 1
#44 enoxaparin* 1914
#45 (clexan* or clexane* or emt-966 or emt-967 or emt966 or emt967 or inhixa* or klexane* or lovenox* or neoparin* or "pk 10 169" or "pk 10169" or pk10169 or "pk10 169" or rp54563 or rp-54563 or thorinane*) 114
#46 (9005-49-6 or 679809-58-6 or 8NZ41MIK1O) 1
#47 tinzaparin* 271
#48 (innohep* or lhn1 or lhn-1 or logiparin*) 89
#49 (9041-08-1 or 3S182ET3UA) 1
#50 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 17727
#51 #5 and #50 2117
#52 #51 Publication Year from 2011 to 2018 1502
#53 #52 in Trials 1256

Source: Google
Interface / URL: https://www.google.co.uk/
Database coverage dates: n/a
Search date: 02/03/18
Retrieved records: 23
Search strategy:

A pragmatic search was conducted to identify relevant research from NHS websites, published from 2011. Results were limited to PDF or Word document types. Searches were constructed using the Google Advanced search interface: https://www.google.ca/advanced_search.

The following 13 searches were conducted individually.

For each search, returned results were rapidly scanned for potentially relevant studies evaluating AF patients' compliance/adherence to anti-coagulants or prescribing patterns for anti-coagulants in AF.

Choice of items to view and selection for further consideration was based on searcher judgement. If links of interest were found in a viewed item, these were followed and additional records viewed if judged to be potentially of interest (even if the additional records were not from NHS sites).

1. allintitle: "atrial fibrillation" site:.nhs.uk filetype:doc
4 results returned and assessed, 0 retrieved for further consideration

2. allintitle: "atrial fibrillation" adherence site:.nhs.uk filetype:pdf
0 results

3. allintitle: "atrial fibrillation" compliance site:.nhs.uk filetype:pdf
0 results

4. allintitle: "atrial fibrillation" prescription site:.nhs.uk filetype:pdf
0 results

5. allintitle: "atrial fibrillation" prescriptions site:.nhs.uk filetype:pdf
0 results

6. allintitle: "atrial fibrillation" prescribing site:.nhs.uk filetype:pdf
6 results returned and assessed, 0 retrieved for further consideration

7. allintitle: "atrial fibrillation" anticoagulant site:.nhs.uk filetype:pdf
3 results returned and assessed, 0 selected

8. allintitle: "atrial fibrillation" anticoagulants site:.nhs.uk filetype:pdf
'About 20 results' returned and assessed, 0 retrieved for further consideration

9. allintitle: "atrial fibrillation" OAC site:.nhs.uk filetype:pdf
0 results

10. allintitle: "atrial fibrillation" OACs site:.nhs.uk filetype:pdf
0 results

11. allintitle: "atrial fibrillation" NOAC site:.nhs.uk filetype:pdf
2 results returned and assessed, 1 retrieved for further consideration

12. allintitle: "atrial fibrillation" NOACs site:.nhs.uk filetype:pdf
3 results returned and assessed, 0 selected

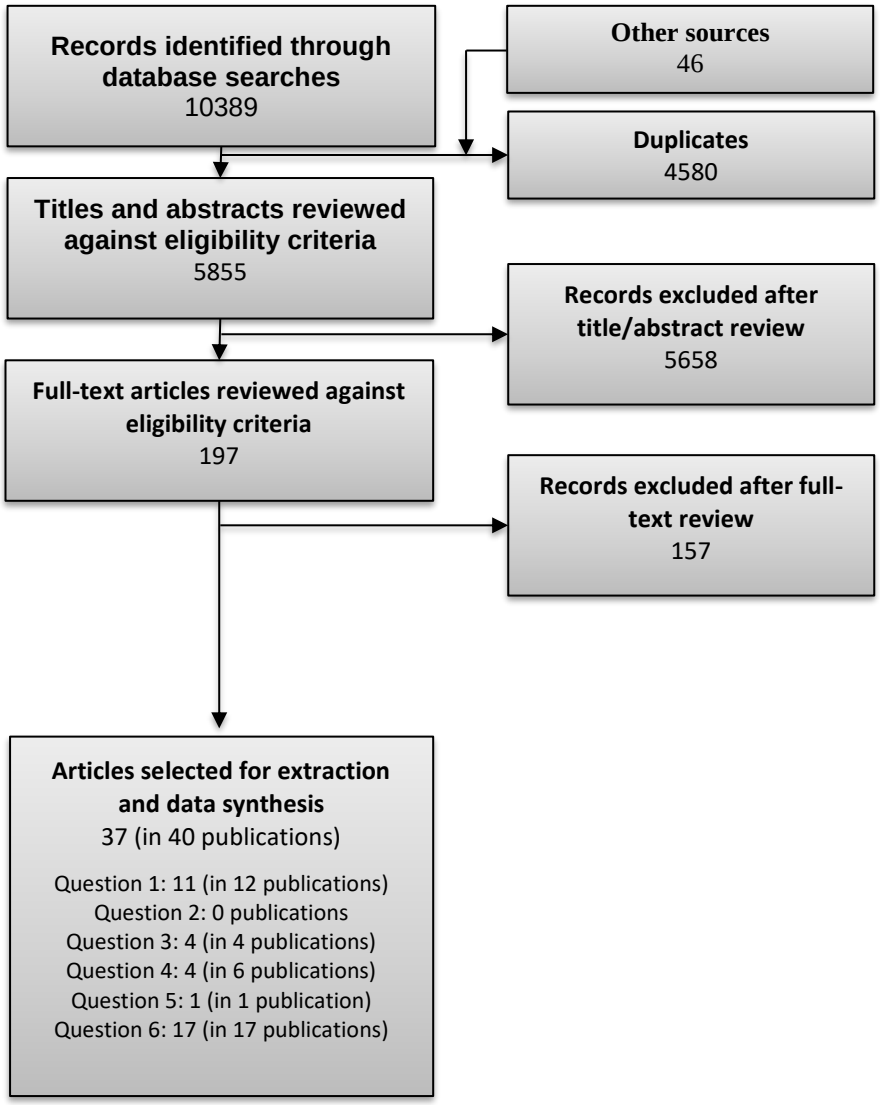
13. allintitle: "atrial fibrillation" site:.nhs.uk filetype:pdf
‘About 303 results’ returned. 22 retrieved for further consideration.

Appendix 2 — Included and excluded studies

PRISMA flowchart

Figure 2.1 summarises the volume of publications included and excluded at each stage of the review. Forty publications were ultimately judged to be relevant to one or more review questions and were considered for extraction. Publications that were included or excluded after the review of full-text articles are detailed below.

Figure 2.1. Summary of publications included and excluded at each stage of the review



Publications included after review of full-text articles

The 40 publications included after review of full-texts are summarised in Table 2.1. Summary oPublications not selected for extraction and data synthesis are detailed in Table 2.2

Table 2.1. Summary of publications included after review of full-text articles, and the question(s) which each publication informed

	Criterion	Key questions	Studies Included
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.	1a. Is the risk of stroke similar between people with paroxysmal AF compared to people with persistent or permanent AF? 1b. Is the risk of stroke similar between people with asymptomatic compared to symptomatic AF?	1a. Al-Khatib 2013 [10]; Banerjee 2013 [11]; Baturova 2014 [12]; Disertori 2013 [13]; Flaker 2012 [14]; Lip 2014 [15, 16]; Meinertz 2011 [17]; Proietti 2017 [18]; Steinberg 2015 [19]; Vanassche 2015 [20]. 1b. Potpara 2013 [21]; Rienstra 2014 [22].
9	There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme shouldn't be further considered.	Question 2a – What is the benefit of treating screen-detected AF? Question 2b – Is there a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?	2a. and 2b. No studies met the inclusion criteria for these questions.

	Criterion	Key questions	Studies Included
4	There should be a simple, safe, precise and validated screening test.	Question 3 – What is the reported accuracy of screening tests for all types of AF?	Hald 2017 [23]; Kristensen 2016 [24]; Svennberg 2017 [25]; Welton 2017 [26].
11	There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity..	Question 4 – Have randomised controlled trials (RCTs) demonstrated a benefit of formal screening programmes for AF over and above diagnosis of AF only through clinical practice?	González Blanco 2017[27]; Halcox 2017 [28]; Moran 2013 [29]; 2015[30]; 2016[9]; Welton 2017 [26].
14	The opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole (value for money). Assessment against this criteria should have regard to evidence from cost benefit and/or cost effectiveness analyses and have regard to the effective use of available resource.	Question 1 – Is screening for AF in adults cost-effective?	Welton 2017 [26]
15	Clinical management of the condition and patient outcomes should be optimised in all health care providers prior to participation in a screening programme.	Question 6a – Is the current clinical pathway for AF optimised in terms of patient compliance? Question 6b – Is the current clinical pathway for AF optimised in terms of prescribing patterns for anticoagulants?	6a. Das 2015 [31]; Hodgkinson 2011 [32]; Johnson 2016 [33]; Martinez 2016 [34]; Mueller 2017 [35]. 6b. Corteville 2015 [36];Das 2015 [31]; Induruwa 2017 [37]; Isaew 2017 [38]; Gallager 2014 [39]; Kerr 2014 [40]; Lonsdale 2016 [41]; Martinez 2016 [34]; Mazurek 2017 [42]; NHS Blackpool ; Quality and Outcomes Framework (QOF) [43-46].

Publications excluded after review of full-text articles

Table 2.2. Publications excluded after review of full-text articles

Reference	Reason for exclusion
Abdou JK, Auyeung V, Patel JP, Arya R. Adherence to long-term anticoagulation treatment, what is known and what the future might hold. British Journal of Haematology. 2016;174(1):30-42.	Ineligible study design
Abdul-Rahim AH, Wong J, McAlpine C, Young C, Quinn TJ. Associations with anticoagulation: A cross-sectional registry-based analysis of stroke survivors with atrial fibrillation. Heart. 2014;100(7):557-62.	Ineligible patient population
Ahmad Y, Lip GYH, Apostolakis S. New oral anticoagulants for stroke prevention in atrial fibrillation: impact of gender, heart failure, diabetes mellitus and paroxysmal atrial fibrillation. Expert Rev Cardiovasc Ther. 2012;10(12):1471-80.	SR, included studies checked
Albert DE. Performance of hand-held electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. Europace. 2017;19(8):1408.	Ineligible study design
Amara W, Larsen TB, Sciaraffia E, Hernandez Madrid A, Chen J, Estner H, et al. Patients' attitude and knowledge about oral anticoagulation therapy: Results of a self-assessment survey in patients with atrial fibrillation conducted by the European Heart Rhythm Association. Europace. 2015;18(1):151-55.	Ineligible study country
Anczykowski J, Willems S, Hoffmann BA, Meinertz T, Blankenberg S, Patten M. Early Detection of Symptomatic Paroxysmal Cardiac Arrhythmias by Trans-Telephonic ECG Monitoring: Impact on Diagnosis and Treatment of Atrial Fibrillation. Journal of Cardiovascular Electrophysiology. 2016;27(9):1032-7.	Ineligible patient population
Andersson P, Londahl M, Abdon NJ, Terent A. The prevalence of atrial fibrillation in a geographically well-defined population in Northern Sweden: Implications for anticoagulation prophylaxis. Journal of Internal Medicine. 2012;272(2):170-76.	Ineligible outcomes
Andersson T, Magnuson A, Bryngelsson IL, Frobert O, Henriksson KM, Edvardsson N, et al. Gender-related differences in risk of cardiovascular morbidity and all-cause mortality in patients hospitalized with incident atrial fibrillation without concomitant diseases: A nationwide cohort study of 9519 patients. International Journal of Cardiology. 2014;177(1):91-99.	Ineligible patient population
Andrade JG, Field T, Khairy P. Detection of occult atrial fibrillation in patients with embolic stroke of uncertain source: A work in progress. Frontiers in Physiology. 2015;6(APR):100.	Ineligible patient population
Antonicelli R, Ripa C, Abbatecola AM, Capparuccia CA, Ferrara L, Spazzafumo L. Validation of the 3-lead tele-ECG versus the 12-lead tele-ECG and the conventional 12-lead ECG method in older people. J Telemed Telecare. 2012;18(2):104-8.	Ineligible outcomes
Auyeung V, Patel JP, Abdou JK, Vadher B, Bonner L, Brown A, et al. Anticoagulated patient's perception of their illness, their beliefs about the anticoagulant therapy prescribed and the relationship with adherence: Impact of novel oral anticoagulant therapy - study protocol for the switching study: A prospective cohort study. BMC Hematology. 2016;16(1):22.	Protocol only
Bai Y, Guo SD, Deng H, Shantsila A, Fauchier L, Ma CS, et al. Effectiveness and safety of oral anticoagulants in older patients with atrial fibrillation: A systematic review and meta-regression analysis. Age and Ageing. 2018;47(1):9-17.	Ineligible patient population
Bandemer SV, Merkel S, Nimako-Doffour A, Weber MM. Diabetes and atrial fibrillation: Stratification and prevention of stroke risks. EPMA Journal. 2014;5(1):17.	Ineligible study design

Barrios V, Escobar C, Baron G, Gomez Doblas JJ, Parici M, Recalde E, et al. Management of oral anticoagulants in outpatients with nonvalvular atrial fibrillation daily attended by cardiologists. Journal of Hypertension 2017; 35: e288. Available from: https://insights.ovid.com/crossref?an=00004872-201709002-00857	Abstract only
Bartoli-Abdou JK, Patel JP, Crawshaw J, Vadher B, Brown A, Roberts LN, et al. Exploration of adherence and patient experiences with DOACs one year after switching from vitamin-K antagonists- insights from the switching study. Thrombosis Research. 2018;162:62-68.	Ineligible outcomes
Basaran O, Filiz Basaran N, Cekic EG, Altun I, Dogan V, Mert GO, et al. PRescriptiOn PattERns of Oral Anticoagulants in Nonvalvular Atrial Fibrillation (PROPER study). Clinical and Applied Thrombosis/Hemostasis. 2017;23(4):384-91.	Ineligible study country
Battipaglia I, Gilbert K, Hogarth AJ, Tayebjee MH. Screening for atrial fibrillation in the community using a novel ECG recorder. Journal of Atrial Fibrillation. 2016;9(2):29-31.	Ineligible study design
Baturova MA, Sheldon SH, Carlson J, Brady PA, Lin G, Rabinstein AA, et al. Electrocardiographic and Echocardiographic predictors of paroxysmal atrial fibrillation detected after ischemic stroke. BMC Cardiovasc Disord. 2016;16(1):209.	Ineligible patient population
Bellew SD, Moman R, Lohse CM, Hess EP, Bellolio MF. Validation of a decision rule for selective TSH screening in atrial fibrillation. Western Journal of Emergency Medicine. 2015;16(1):195-202.	Ineligible patient population
Berge T, Brynildsen J, Larssen HKN, Onarheim S, Jenssen GR, Ihle-Hansen H, et al. 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. 2017;31:31.	Abstract only
Borg Xuereb C, Shaw RL, Lane DA. Patients' and health professionals' views and experiences of atrial fibrillation and oral-anticoagulant therapy: A qualitative meta-synthesis. Patient Education and Counseling. 2012;88(2):330-37.	Ineligible outcomes
Brunetti ND, De Gennaro L, Pellegrino PL, Dellegrottaglie G, Antonelli G, Di Biase M. Atrial fibrillation with symptoms other than palpitations: Incremental diagnostic sensitivity with at-home tele-cardiology assessment for emergency medical service. European Journal of Preventive Cardiology. 2012;19(3):306-13.	Ineligible study design
Bury G, Swan D, Cullen W, Keane D, Tobin H, Egan M, et al. Screening for atrial fibrillation in general practice: A national, cross-sectional study of an innovative technology. International Journal of Cardiology. 2015;178:247-52.	Ineligible study design
Campbell EB, Johnsson K, Lejonberg C. Detection of paroxysmal atrial fibrillation in acute stroke/TIA patients using a 21 day monitoring device, RTest 4. Cerebrovascular diseases (Basel, Switzerland). 2015; (Suppl 2): 172. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/791/CN-01101791/frame.html	Abstract
Carpenter A, Frontera A. Smart-watches: a potential challenger to the implantable loop recorder? 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. 2016;18(6):791-93.	Ineligible study design
CCG NCaP. CVD: Primary Care Intelligence Packs. June 2017. Version 1. NHS Cambridgeshire and Peterborough CCG. London: Public Health England; 2017. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/623317/NHS_Cambridgeshire_and_Peterborough_CCG_CVD_intelligence_pack.pdf.	Ineligible outcomes
CCG NCaP. Effective Treatment of Atrial Fibrillation to Prevent Strokes Event. Data Pack. Cambridgeshire and Peterborough CCG. 2017. London: Public Health England; 2017. Available from:	Ineligible study design

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Chan P-H, Wong C-K, Pun L, Wong Y-F, Wong MM-Y, Chu DW-S, et al. Diagnostic performance of an automatic blood pressure measurement device, Microlife WatchBP Home A, for atrial fibrillation screening in a real-world primary care setting. BMJ Open. 2017;7(6):e013685.	Ineligible study country
Chanda A, Wolff A, McPherson C, Kwon J. Utility of extended cardiac monitoring to detect atrial fibrillation in patients with severe obstructive sleep apnea. Sleep and Breathing. 2015;19(1):407-10.	Ineligible patient population
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Chen J-Y, Zhang A-D, Lu H-Y, Guo J, Wang F-F, Li Z-C. CHADS2 versus CHA2DS2-VASc score in assessing the stroke and thromboembolism risk stratification in patients with atrial fibrillation: a systematic review and meta-analysis. Journal of Geriatric Cardiology. 2013;10(3):258-66.	Duplicate
Cheng HM, Tufanaru C, Pearson A, Chen CH. Automated blood pressure measurement in atrial fibrillation: A systematic review and meta-analysis. Journal of Hypertension. 2013;31(1):214-15.	Ineligible intervention
Chung EH, Guise KD. QTC intervals can be assessed with the AliveCor heart monitor in patients on dofetilide for atrial fibrillation. Journal of Electrocardiology. 2015;48(1):8-9.	Ineligible study design
Cifu A, Prasad V. Wearables, Smartphones and Novel Anticoagulants: We Will Treat More Atrial Fibrillation, but Will Patients Be Better Off? Journal of General Internal Medicine. 2016;31(11):1367-68.	Ineligible study design
Clarkesmith DE, Lip GYH, Lane DA. Patients' experiences of atrial fibrillation and non-vitamin K antagonist oral anticoagulants (NOACs), and their educational needs: A qualitative study. Thrombosis Research. 2017;153:19-27.	Ineligible study design
Conroy T, Guzman JH, Hall B, Tsouri G, Couderc J-P. Detection of atrial fibrillation using an earlobe photoplethysmographic sensor. Physiol Meas. 2017;38(10):1906-18.	Ineligible patient population
Corino VDA, Laureanti R, Ferranti L, Scarpini G, Lombardi F, Mainardi LT. Detection of atrial fibrillation episodes using a wristband device. Physiol Meas. 2017;38(5):787-99.	Ineligible outcomes
Couderc JP, Kyal S, Mestha LK, Xu B, Peterson DR, Xia X, et al. Detection of atrial fibrillation using contactless facial video monitoring. Heart rhythm. 2015; (1): 195-201. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/086/CN-01114086/frame.html	Ineligible patient population
Dagres N, Varounis C, Iliodromitis EK, Lekakis JP, Rallidis LS, Anastasiou-Nana M. Dronedarone and the incidence of stroke in patients with paroxysmal or persistent atrial fibrillation: A systematic review and meta-analysis of randomized trials. American Journal of Cardiovascular Drugs. 2011;11(6):395-400.	Ineligible intervention

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Davis RC, Hobbs FDR, Kenkre JE, Roalfe AK, Iles R, Lip GYH, et al. Prevalence of atrial fibrillation in the general population and in high-risk groups: The ECHOES study. Europace. 2012;14(11):1553-59.	Ineligible outcomes
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Derkac WM, Finkelmeier JR, Horgan DJ, Hutchinson MD. Diagnostic yield of asymptomatic arrhythmias detected by mobile cardiac outpatient telemetry and autotrigger looping event cardiac monitors. Journal of Cardiovascular Electrophysiology. 2017;28(12):1475-78.	Ineligible intervention
Desteghe L, Raymaekers Z, Lutin M, Vijgen J, Dilling-Boer D, Koopman P, et al. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. Europace. 2017;19(1):29-39.	Ineligible patient population
Desteghe L, Raymaekers Z, Vijgen J, Dilling-Boer D, Koopman P, Schurmans J, et al. Accuracy and usability of handheld electrocardiogram recorders to detectatrial fibrillation in hospitalised patients. Europace. Conference: world congress in cardiac electrophysiology and cardiac techniques 2016. France. 2016; 18(Suppl 1): i177. Available from: https://academic.oup.com/europace/article/18/suppl_1/i1/2802525	Abstract only
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Engdahl J, Holmen A, Svennberg E, Friberg L, Frykman-Kull V, Al-Khalili F, et al. Geographic and socio-demographic differences in uptake of population-based screening for atrial fibrillation: The STROKESTOP I study. International Journal of Cardiology. 2016;222:430-35.	Ineligible outcomes
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Fay MR, Fitzmaurice DA, Freedman B. Screening of older patients for atrial fibrillation in general practice: Current evidence and its implications for future practice. Eur J Gen Pract. 2017;23(1):246-53.	Ineligible study design
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Fitch K, Broulette J, Pyenson BS, Iwasaki K, Kwong WJ. Utilization of anticoagulation therapy in medicare patients with nonvalvular atrial fibrillation. American Health and Drug Benefits. 2012;5(3):157-68.	Ineligible study design
Friberg L, Hammar N, Rosenqvist M. Stroke in paroxysmal atrial fibrillation: report from the Stockholm Cohort of Atrial Fibrillation. Eur Heart J. 2010;31(8):967-75.	Ineligible date

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Gill PS, Calvert M, Davis R, Davies MK, Freemantle N, Lip GYH. Prevalence of heart failure and atrial fibrillation in minority ethnic subjects: The Ethnic-Echocardiographic heart of England screening study (E-ECHOES). PLoS ONE. 2011;6(11):e26710.	Ineligible outcomes
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Hobbs FD, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess. 2005;9(40):iii-iv, ix-x, 1-74.	Duplicate
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Howlett P, Hickman M, Leatham E. Calling the cardioverted: An audit of long-term anticoagulation in patients attending for DCCV. British Journal of Cardiology. 2015;22(3):114-17.	Ineligible intervention
Hsu JC, Chan PS, Tang F, Maddox TM, Marcus GM. Differences in anticoagulant therapy prescription in patients with paroxysmal versus persistent atrial fibrillation. American Journal of Medicine. 2015;128(6):654.e1-54.e10.	Ineligible patient population
Jaakkola J, Virtanen R, Vasankari T, Salminen M, Airaksinen KEJ. Self-detection of atrial fibrillation in an aged population - The lietoaf study. Circulation. 2016; 134(Suppl 1): A17869. Available from: http://circ.ahajournals.org/content/134/Suppl_1/A17869	Abstract only
Jaakkola J, Virtanen R, Vasankari T, Salminen M, Airaksinen KEJ. Self-detection of atrial fibrillation in an aged population: three-year follow-up of the LietoAF intervention study. BMC geriatr. 2017;17(1):218.	Ineligible outcomes
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Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: A systematic review and meta-analysis. Stroke. 2014;45(2):520-26.	Ineligible patient population
Koga M, Yoshimura S, Hasegawa Y, Shibuya S, Ito Y, Matsuoka H, et al. Higher Risk of Ischemic Events in Secondary Prevention for Patients with Persistent Than Those with Paroxysmal Atrial Fibrillation. Stroke. 2016; (10): 2582-88. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/350/CN-01193350/frame.html http://stroke.ahajournals.org/content/strokeaha/47/10/2582.full.pdf	Ineligible study country
Komocsi A. Discontinuation of anticoagulant treatment: From clinical trials to medication persistence. Current Medical Research and Opinion. 2015;31(10):1841-44.	Ineligible outcomes
Kvist TV, Lindholt JS, Rasmussen LM, Sogaard R, Lambrechtsen J, Steffensen FH, et al. The DanCavas Pilot Study of Multifaceted Screening for Subclinical Cardiovascular Disease in Men and Women Aged 65-74 Years. European Journal of Vascular and Endovascular Surgery. 2017;53(1):123-31.	Ineligible intervention
Lahdenoja O, Hurnanen T, Iftikhar Z, Nieminen S, Knuutila T, Saraste A, et al. Atrial Fibrillation Detection via Accelerometer and Gyroscope of a Smartphone. IEEE Journal of Biomedical and Health Informatics. 2018;22(1):108-18.	Ineligible outcomes

Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, Galloway CD, et al. iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke. Int J Cardiol. 2013;165(1):193-4.	Ineligible outcomes
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Lee J, Reyes BA, McManus DD, Mathias O, Chon KH. Atrial fibrillation detection using an iphone 4S. IEEE Transactions on Biomedical Engineering. 2013;60(1):203-06.	Abstract
Leiden University Medical Center. Mobile phones in cryptogenic stroke patients bringing single lead ECGs to detect atrial fibrillation (MOBILE-AF). In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2017. Available from https://clinicaltrials.gov/ct2/show/NCT02507986.	Ineligible patient population
Limone BL, Baker WL, Kluger J, Coleman CI. Novel Anticoagulants for Stroke Prevention in Atrial Fibrillation: A Systematic Review of Cost-Effectiveness Models. PLoS ONE. 2013;8(4):e62183.	Ineligible patient population
Linker DT. Accurate, Automated Detection of Atrial Fibrillation in Ambulatory Recordings. Cardiovascular Engineering and Technology. 2016;7(2):182-89.	Ineligible patient population
Lip GYH, Laroche C, Boriani G, Dan GA, Santini M, Kalarus Z, et al. Regional differences in presentation and treatment of patients with atrial fibrillation in Europe: A report from the EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. Europace. 2014;17(2):194-206.	Ineligible study country
Lip GYH, Laroche C, Dan GA, Santini M, Kalarus Z, Rasmussen LH, et al. 'Real-World' antithrombotic treatment in atrial fibrillation: The eorp-af pilot survey. American Journal of Medicine. 2014;127(6):519-29.e1.	Ineligible study country
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Lopes LC, Spencer FA, Neumann I, Ventresca M, Ebrahim S, Zhou Q, et al. Systematic review of observational studies assessing bleeding risk in patients with atrial fibrillation not using anticoagulants. PLoS ONE. 2014;9(2):e88131.	Ineligible outcomes
Lopez-Lopez JA, Sterne JAC, Thom HHZ, Higgins JPT, Hingorani AD, Okoli GN, et al. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. BMJ (Clinical research ed.). 2017;359:j5058.	Ineligible patient population
Lown M, Yue A, Lewith G, Little P, Moore M. Screening for Atrial Fibrillation using Economical and accurate Technology (SAFETY)-a pilot study. BMJ Open. 2017;7(1):e013535.	Protocol only
Lowres N, Neubeck L, Redfern J, Freedman SB. Screening to identify unknown atrial fibrillation. A systematic review. Thromb Haemost. 2013;110(2):213-22.	Ineligible outcomes
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Martinez C, Katholing A, Freedman SB. Adverse prognosis of incidentally detected ambulatory atrial fibrillation. Thrombosis and Haemostasis. 2014;112(2):276-86.	Ineligible comparator
Mas Dalmau G, Sant Arderiu E, Enfedaque Montes MB, Sola I, Pequeno Saco S, Alonso Coello P. Patients' and physicians' perceptions and attitudes about oral anticoagulation and atrial fibrillation: a qualitative systematic review. BMC family practice. 2017;18(1):3.	Ineligible outcomes
Mazurek M, Huisman MV, Lip GYH. Registries in Atrial Fibrillation: From Trials to Real-Life Clinical Practice. American Journal of Medicine. 2017;130(2):135-45.	Ineligible study country
McCahon D, Fitzmaurice DA, Baker J, Murray ET, Jowett S, Sandhar H, et al. Atrial fibrillation: is screening effective in identifying patients at risk of stroke? British journal of haematology. 2014; 165(Suppl. 1): 10-11. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/bjh.12802	Abstract only
Miedel C, Leander K, de Faire U, Gigante B. Pulse pressure is not an independent predictor of incident atrial fibrillation in 60-year-old men and women. Ann Med. 2015;47(8):679-86.	Ineligible outcomes
Moran P, Teljeur C, Harrington P, Smith S, Normand C, Ryan M. Opportunistic Screening For Atrial Fibrillation In Primary Care - A Clinical And Cost-Effectiveness Analysis. Value in Health. 2015;18(7):A391.	Abstract
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O'Dell KM, Igawa D, Hsin J. New Oral Anticoagulants for Atrial Fibrillation: A Review of Clinical Trials. Clinical Therapeutics. 2012;34(4):894-901.	Ineligible patient population
Overgaard MS, Christensen LM, R SR, Overgaard K, Christensen H. The challenge of detecting atrial fibrillation a literature based review on current studies. Cerebrovascular diseases. 2013; 35: 818. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/700/CN-01023700/frame.html	Abstract
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Poppe KK, Doughty RN, Harwood M, Barber PA, Harrison J, Jackson R, et al. Identification, risk assessment, and management of patients with atrial fibrillation in a large primary care cohort. International Journal of Cardiology. 2018;254:119-24.	Ineligible intervention
Population Health Research Institute. Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation. In: ClinicalTrials.gov [internet]. Bethesda: US National Library of Medicine: 2015. Available from Http://clinicaltrials.gov/show/nct01938248.	Protocol only
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Public Health England. Systematic population screening programme not recommended, clinical practice guidelines covered by NICE. London: Public Health England; July 2014. Available from: https://legacyscreening.phe.org.uk/atrialfibrillation.	SR, included studies checked
Pugh D, Pugh J, Mead GE. Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review. Age Ageing. 2011;40(6):675-83.	Ineligible outcomes
Queiroz JA, Junior A, Lucena F, Barros AK. Diagnostic decision support systems for atrial fibrillation based on a novel electrocardiogram approach. Journal of Electrocardiology. 2017;51(2):252-59.	Ineligible intervention
Rangel MO, O'Neal WT, Soliman EZ. Usefulness of the Electrocardiographic P-Wave Axis as a Predictor of Atrial Fibrillation. American Journal of Cardiology. 2016;117(1):100-4.	Ineligible study design
Rosenqvist M. Systematic ECG Screening for Atrial Fibrillation Among 75 Year Old Subjects in the Region of Stockholm and Halland, Sweden. 2012: Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/969/CN-01014969/frame.html	Protocol only
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Schaefer JR, Leussler D, Rosin L, Pittrow D, Hepp T. Improved detection of paroxysmal atrial fibrillation utilizing a software-assisted electrocardiogram approach. PLoS ONE. 2014;9(2):e89328.	Ineligible patient population
Steinberg BA, Hellkamp AS, Lokhnygina Y, Patel MR, Breithardt G, Singer DE, et al. Higher risk of death and stroke in patients with persistent versus paroxysmal atrial fibrillation: results from the ROCKET AF trial. European heart journal. 2014; 35(Suppl 1): 866. Available from: https://academic.oup.com/eurheartj/article/35/suppl_1/851/541962	Abstract only
Steinhubl SR, Mehta RR, Ebner GS, Ballesteros MM, Waalen J, Steinberg G, et al. Rationale and design of a home-based trial using wearable sensors to detect asymptomatic atrial fibrillation in a targeted population: The mHealth Screening To Prevent Strokes (mSToPS) trial. Am Heart J. 2016;175:77-85.	Abstract only
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Sterne JAC, Bodalia PN, Bryden PA, Davies PA, Lopez-Lopez JA, Okoli GN, et al. Oral anticoagulants for primary prevention, treatment and secondary prevention of venous thromboembolic disease, and for prevention of stroke in atrial	Ineligible patient population

fibrillation: Systematic review, network meta-analysis and cost-effectiveness analysis. Health Technology Assessment. 2017;21(9):1-385.	
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Svennberg CE, Engdahl J, Frykman-Kull V, Friberg L, Levin LA, Rosenqvist M. Mass screening for silent atrial fibrillation in high risk patients - preliminary results from the STROKESTOP trial. European heart journal. 2013; (suppl 1): 809. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/911/CN-00982911/frame.html	Abstract only
Svennberg CE, Engdahl J, Frykman-Kull V, Friberg L, Levin LA, Rosenqvist M. Population screening of 75-year-old individuals for silent atrial fibrillation - preliminary data from the STROKESTOP trial. Cerebrovascular diseases (Basel, Switzerland). 2013; (Suppl 3): 126. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/912/CN-00982912/frame.html	Abstract only
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Svennberg E, Henriksson P, Engdahl J, Hijazi Z, Al-Khalili F, Friberg L, et al. N-terminal pro B-type natriuretic peptide in systematic screening for atrial fibrillation. Heart. 2017;103(16):1271-77.	Ineligible intervention
Taggar JS, Coleman T. Screening for atrial fibrillation in primary care: From recommendation to implementation. European Journal of Preventive Cardiology. 2016;23(17):1880-82.	Ineligible study design
Taggar JS, Coleman T, Lewis S, Heneghan C, Jones M. Accuracy of methods for diagnosing atrial fibrillation using 12-lead ECG: A systematic review and meta-analysis. Int J Cardiol. 2015;184:175-83.	Ineligible intervention
Tawfik A, Bielecki JM, Krahn M, Dorian P, Hoch JS, Boon H, et al. Systematic review and network meta-analysis of stroke prevention treatments in patients with atrial fibrillation. Clinical Pharmacology: Advances and Applications. 2016;8:93-107.	Ineligible patient population
Teutsch C, Huisman MV, Lip GYH, Diener HC, Dubner SJ, Changsheng M, et al. Persistence with dabigatran therapy for stroke prevention in patients with non-valvular atrial fibrillation: the Gloria-AF Registry. Blood. 2016; 128(22): 2616. Available from: http://www.bloodjournal.org/content/128/22/2616	Abstract
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Uittenbogaart SB, Verbiest-van Gurp N, Erkens PMG, Lucassen WAM, Knottnerus JA, Winkens B, et al. Detecting and Diagnosing Atrial Fibrillation (D<inf>2</inf>AF): Study protocol for a cluster randomised controlled trial. Trials. 2015;16(1):478.	Protocol only
UMC Utrecht. Improving DEtection of Atrial fibriLlation in Primary Care With the MyDiagnostick. Bethesda: US National Library of Medicine: 2014. Available from Http://clinicaltrials.gov/show/nct02270151.	Protocol only
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;203:465-73.	SR, included studies checked
Vimalesvaran K, Dockrill SJ, Gorog DA. Role of rivaroxaban in the management of atrial fibrillation: Insights from clinical practice. Vascular Health and Risk Management. 2018;14:13-21.	Ineligible study design
Waring OAW, Davidson NCD, Stout MS, Pearce KP. Detection of atrial fibrillation in community locations using novel technology's as a method of stroke prevention in the over 65's asymptomatic population - Should it become standard	Abstract only

practise? Europace. Conference: heart rhythm congress 2016. United kingdom. 2016; 18(Suppl 2): ii39. Available from: https://academic.oup.com/europace/article/18/suppl_2/ii36/2473764	
Welton N. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis (Project record). Health Technology Assessment Database. 2015; (4): Available from: http://onlinelibrary.wiley.com/o/cochrane/clhta/articles/HTA-32015000762/frame.html	Duplicate
Weymann A, Ali-Hasan-Al-Saegh S, Sabashnikov A, Popov A-F, Mirhosseini SJ, Liu T, et al. Prediction of New-Onset and Recurrent Atrial Fibrillation by Complete Blood Count Tests: A Comprehensive Systematic Review with Meta-Analysis. Med Sci Monit Basic Res. 2017;23:179-222.	Ineligible intervention
Wiesel J, Arbesfeld B, Schechter D. Comparison of the microlife blood pressure monitor with the omron blood pressure monitor for detecting atrial fibrillation. American Journal of Cardiology. 2014;114(7):1046-48.	Ineligible patient population
Williams J, Pearce K, Benett I. The effectiveness of a mobile ECG device in identifying AF: Sensitivity, specificity and predictive value. British Journal of Cardiology. 2015;22(2):70-72.	Ineligible patient population
Willits I, Keltie K, Craig J, Sims A. WatchBP Home A for opportunistically detecting atrial fibrillation during diagnosis and monitoring of hypertension: A NICE medical technology guidance. Applied Health Economics and Health Policy. 2014;12(3):255-65.	Ineligible study design
Winkler S, Axmann C, Schannor B, Kim S, Leuthold T, Scherf M, et al. Diagnostic accuracy of a new detection algorithm for atrial fibrillation in cardiac telemonitoring with portable electrocardiogram devices. Journal of Electrocardiology. 2011;44(4):460-64.	Ineligible patient population
Xu WW, Hu SJ, Wu T. Risk analysis of new oral anticoagulants for gastrointestinal bleeding and intracranial hemorrhage in atrial fibrillation patients: a systematic review and network meta-analysis. Journal of Zhejiang University: Science B. 2017;18(7):567-76.	Ineligible patient population
Zink MD, Marx N, Crijns HJGM, Schotten U. Opportunities and challenges of large-scale screening for atrial fibrillation. Herzschrittmach. 2018;29(1):57-61.	Ineligible study design
Zweibel S, Trelfa M. The use of mobile cardiac telemetry to improve diagnostic accuracy and enable more efficient patient care. US Cardiology. 2012;9(1):43-46.	Ineligible study design

Appendix 3 — Summary and appraisal of individual studies

Data Extraction

Question 1

Table 3.1. Studies relevant to criterion 1 (question 1a): study characteristics

Reference	Study design	Objective of publication	Data source and country	Data collection	Population
Al-Khatib 2013 [10, 74]	Subgroup analysis from a double-blind, placebo controlled RCT	To conduct a pre-specified secondary analysis of the ARISTOTLE trial to compare outcomes and treatment effect of apixaban vs. warfarin by AF type and duration.	Data from ARISTOTLE a study in 1034 clinical sites in 39 countries	Dec 2006 to April 2010 (*follow-up data were presented up to 30 months)*	18,201 patients with paroxysmal, persistent or permanent AF.
Banerjee 2013 [11]	Retrospective Cohort	To analyse a large hospitalised cohort of patients with non-valvular atrial fibrillation (NVAF) to: (a) whether pattern of NVAF was an independent risk factor for stroke/TE, bleeding and mortality in this cohort; and (b) the differences in risk factor profile and outcome between different patterns of NVAF.	Data from a four-hospital-institution, France	Data from 2001 to 2010 were included.	7,156 patients with non-valvular atrial fibrillation (NVAF) or atrial flutter.

Reference	Study design	Objective of publication	Data source and country	Data collection	Population
Baturova 2014 [12]	Case-control (*subgroup data extracted in patients with AF*)	To assess the prevalence of atrial fibrillation (AF) prior to first-ever ischemic stroke by examining a comprehensive electronic ECG archive.	The Lund Stroke Register (LSR), Sweden	March 2001 to February 2002	336 consecutive stroke patients and 336 age- and gender-matched controls without stroke history. *153 patients with AF*
Disertori 2013 [13, 75]	Subgroup analysis from a double-blind, placebo controlled RCT	To assess the incidence of thromboembolic events in paroxysmal and persistent AF.	Data from the GISSI-AF trial conducted in 114 centres in Europe.	Nov 2004 to Jan 2007; follow-up was 1 year	1,442 patients with sinus rhythm for at least days prior to randomisation into the trial.
Flaker 2012 [14, 76]	Subgroup analysis from a RCT	To compare the effect of two doses of dabigatran etexilate with warfarin in patients with paroxysmal, persistent, and permanent AF.	Data from the RE-LY trial, conducted in 44 countries	2005 to 2007; mean follow-up was 2 years	18,107 patients with AF.
Lip 2014; Proietti 2017 [15, 16]	Prospective cohort	To present the 1-year (Lip 2014) and 2-year (Proietti 2017) data from the EORP-AF Pilot Registry, specifically focusing on symptoms, use of antithrombotic therapy, and rate vs. rhythm strategies, as well as determinants of mortality and stroke.	EURObservational Research Programme-Atrial Fibrillation General Registry (pilot phase); data from nine member European Society of Cardiology (ESC) countries	Enrolment from February 2012 to March 2013 with 1 year follow-up data (Lip 2014) and 2 year follow-up data (Proietti 2017*)*	3,119 patients with AF – consecutive in- and out-patients with AF presenting to cardiologists in 9 of the participating ESC countries
Meinertz 2011 [17]	Prospective cohort (*baseline data only)*	This prospective German ATRIUM registry aimed to characterise AF management in patients treated by primary care physicians.	ATRIUM (Outpatient Registry Upon Morbidity of Atrial Fibrillation) enrolled patients from 730 primary care practices in Germany	Patients were enrolled in 2009	3,667 patients with AF

Reference	Study design	Objective of publication	Data source and country	Data collection	Population
Steinberg 2015 [19]	Subgroup *post hoc* analysis from a double-blind, placebo controlled RCT	To compare outcomes in patients with persistent vs. paroxysmal AF receiving oral anticoagulation.	Data from ROCKET-AF cohort (45 countries worldwide)	December 2006 to September 2010 (*follow-up data were presented up to 30 months)*	14,062 patients with non-valvular AF at high risk of stroke (baseline data from patients who had to have electocardiographic evidence of AF within 30 days prior to randomisation into the ROCKET-AF trial, and medical evidence of AF within the previous year)
Vanassche 2015 [20, 77, 78]	Subgroup analysis from two double-blind, placebo controlled RCTs	To investigate whether the pattern of AF is associated with the risk of stroke based on pooled data on aspirin treated patients.	Pooled data on aspirin-treated patients from ACTIVE-A and AVERROES databases (multi-country)	AVERROES: September 2007 to December 2009; mean follow up 1.1 years ACTIVE A: June 2005 to May 2006; median follow up 3.6 years	6,573 aspirin-treated patients with AF

AF: Atrial fibrillation; ECG: electrocardiogram; RCT: Randomised controlled trial; TE: Thromboembolism

Table 3.2. Studies relevant to criterion 1 (question 1a): outcomes

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
Al-Khatib 2013 [10] Subgroup analysis from a RCT (*follow-up data were presented up to 30 months)*	Paroxysmal AF: n/N=2786/18201 (15.3%)	Paroxysmal AF was defined as recurrent AF that terminates spontaneously, persistent AF was defined as AF that is sustained beyond 7 days, and permanent AF was defined as long-standing AF in which restoring and/or maintaining sinus rhythm has failed or has been foregone.	Median age (25^{th}, 75^{th}): 69 (61, 75) years % male: 58%	**Stroke or systematic embolism** number of events (%/100 patient years): 51 (1.0%)	Mean $CHADS_2$ score: 2.0 (SD1.1)	**All-cause mortality** number of events (%/100 patient years): 149 (2.8%)
	Persistent or permanent AF: n/N=15412/18201 (84.7%)		Median age (25^{th}, 75^{th}): 70 (63, 76) years, p<0.001 % male: 66%, p<0.001	**Stroke or systematic embolism** number of events (%/100 patient years): 426 (1.5%) Unadjusted HR: 0.65 (95% CI: 0.48, 0.87), p=0.003	Mean $CHADS_2$ score: 2.1 (SD 1.1), p<0.001	**All-cause mortality** number of events (%/100 patient years): 1123 (3.9%) Unadjusted HR: 0.72 (95% CI: 0.61, 0.85), p=0.0002
Banerjee 2013 [11] Retrospective cohort *(data collected between 2000 and 2010)*	Paroxysmal AF: n/N=4176/7156 (58.4%)	Paroxysmal NVAF was defined as self-terminating episodes of AF (usually within 7 days), whilst persistent NVAF is present when an NVAF episode either lasts longer than 7 days or requires termination by cardioversion, either with drugs or by direct current cardioversion; long-standing persistent NVAF has lasted for ≥1 year when it is decided to adopt a rhythm control strategy. Permanent NVAF exists when the presence of the arrhythmia is accepted by	Mean age: 68.0 (SD 16.2) years % male: 58%	**Ischaemic stroke** events/event rate: 192, 0.46 (0.40, 0.53) **Stroke/TE** events/event rate: 287, 0.69 (0.61, 0.77)	% with $CHADS_2$ score ≥2: 2080 (49.8%) % with CHA_2DS_2-VAS_C score ≥2 (high risk): 3080 (73.7%)	**All-cause mortality** events/event rate: 414, 0.99 (0.9, 1.09)
	Persistent AF: n/N=376/7156 (5.3%)		Mean age: 67.4 (SD 12.1) years, p=0.98 (compared with paroxysmal) % male: 70%, p<0.001	**Ischaemic stroke** events/event rate: 17, 0.45 (0.26, 0.72), (p=0.54 compared with paroxysmal, HR not reported)	% with $CHADS_2$ score ≥2: 181 (48.1%), p=0.70 (compared with paroxysmal)	**All-cause mortality** events/event rate: 43, 1.14 (0.83, 1.54), (p=0.20 compared with paroxysmal)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
		the patient (and physician) and it has been present for ≥1 year.		**Stroke/TE** events/event rate: 26, 0.69 (0.45, 1.01), (p=0.52 compared with paroxysmal, HR not reported)	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 285 (75.8%), p=0.04	
	Permanent AF: n/N=2604/7156 (36.3%)		Mean age: 73.7 (SD 12.9) years p<0.001 (compared with paroxysmal) % male: 68%, p<0.001	**Ischaemic stroke** events/event rate: 153, 0.59 (0.5, 0.69), (p=0.01 compared with paroxysmal, HR not reported) **Stroke/TE** events/event rate: 26, 0.89 (0.78, 1.01), (p=0.001 compared with paroxysmal, HR not reported)	% with $CHADS_2$ score ≥2: 1556 (59.8%), p=0.008 (compared with paroxysmal) % with CHA_2DS_2-VAS_C score ≥2 (high risk): 2200 (84.5%), p=0.02	**All-cause mortality** events/event rate: 390, 1.50 (1.35, 1.65), (p<0.001 compared with paroxysmal)
Baturova 2014 [12] Case-control (*subgroup data extracted in patients with AF*)	Non-permanent AF: n/N = 100/153 (65.4%)	AF was defined as non-permanent when it was considered paroxysmal or persistent (with consecutive cardioversion) by the attending physician or when spontaneous conversion to sinus rhythm was proven by the ECG with sinus rhythm at	M Median age: 80 (IQ 13) years *(no other baseline characteristics reported for the subgroup of patients with AF)*	Stroke data not reported as all patients has a stroke at baseline. The authors only presented information on stroke severity measured by the NIHSS scale:	Median $CHADS_2$ score: 2 (IQ 2)	NR

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
(*data from a cohort of stroke patients so no follow-up)*	Permanent AF: n/N = 53/153 (34.6%)	inclusion. Patients who had AF diagnosis in the Swedish Hospital Discharge Register and had sinus rhythm at admission were considered having non-permanent AF. Permanent AF was diagnosed in accordance with documentation in medical records, or when serial ECGs demonstrated arrhythmia without intervening sinus rhythm, including admission ECG.	Median age: 84 (IQ 10) years, p=0.002	Non-permanent median score 5 (IQ 12) vs permanent median score 4 (IQ 11), p=0.941	Median $CHADS_2$ score: 2 (IQ 3), p=0.039	
Disertori 2013 [13] Subgroup analysis from a RCT (*1 year follow-up)*	Paroxysmal AF: n/N=771/1442 (53.5%)	AF was defined as paroxysmal if the AF was self-terminating, usually within 48 hours, although AF could continue for up to 7 days; AF was defined as persistent when the AF episodes lasted longer than 7 days. Arrhythmia termination by cardioversion did not change the classification of AF.	Mean age: 66.8 (SD 9.8) years % male: 55%	**Thromboembolic events** 6 (0.8%)	% with $CHADS_2$ score ≥2: 268 (34.8%)	**Death** 9 (1.2%)
	Persistent AF: n/N=463/1442 (32.1%) *Categorisation was not made in the remaining 14.4% of patients*		Mean age: 68.8 (SD 8.5) years, p=0.0002 % male: 71%, p<0.0001	**Thromboembolic events** 6 (1.3%) Adjusted HR 2.14 (95% CI: 0.68, 6.79), p=0.20	% with $CHADS_2$ score ≥2: 174 (37.6%)	**Death** 3 (0.65%) Adjusted HR 0.52 (95% CI: 0.13, 1.03), p=0.35

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
Flaker 2012 [14] Subgroup analysis from a RCT (*mean follow-up 2 years)*	Paroxysmal AF: n/N=5943/18107 (32.8%) Persistent AF: n/N=5789/18107 (32.0%) Permanent AF: n/N=6375/18107 (35.2%)	Not reported	Not reported by type of AF	**Stroke or systemic embolism** 1.32% per year **Stroke or systemic embolism** 1.55% per year **Stroke or systemic embolism** 1.49% per year (*no statistical comparisons were reported*)	Not reported by type of AF	Not reported by type of AF
Lip 2014 (*1 year follow-up*); Proietti 2017 [18] *(2 year follow-up)* Prospective cohort *(up to 2 years follow-up)*	Paroxysmal AF: n/N=693/2589 (26.8%)	Not reported	Mean age: 66.7 years (SD 11.4) % male: 58%	**Readmissions for stroke** 1 year: 2/627 2 years: 1/495 (*denominators are not clear – we have extracted data on what appears to be the total number of readmissions within each group*)	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 506 (73.0%)	**Ischaemic/haemorrhagic stroke death** 1 year: 2/808 2 years: - (*denominators are not clear – we have extracted data on what appears to be all participants enrolled within each group*)
	Persistent AF: n/N=550/2589 (21.2%)		Mean age: 67.9 years (SD 11.0) % male: 60%	**Readmissions for stroke** 1 year: 2/477 2 years: 0/363	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 447 (81.3%)	**Ischaemic/haemorrhagic stroke death** 1 year: 1/647 2 years: 1/430

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
	Long-standing persistent AF: n/N=121/2589 (4.7%)		Mean age: 70.9 years (SD 10.8) % male: 61%	**Readmissions for stroke** 1 year: 0/73 2 years: 0/82	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 107 (88.4%)	**Ischaemic/haemorrhagic stroke death** 1 year: 4/145 2 years: -
	Permanent AF: n/N=451/ 2589 (17.4%)		Mean age: 73.0 years (SD 10.2) % male: 58%	**Readmissions for stroke** 1 year: 4/382 2 years: 5/309	% with CHA_2DS_2-VAS_C score ≥2 (high risk): 417 (92.5%)	**Ischaemic/haemorrhagic stroke death** 1 year: 1/526 2 years: -
Meinertz 2011 [17] Prospective cohort (*baseline data only*)	Paroxysmal AF: n/N=994/3667 (26%)	Not reported	Mean age: 69.8 (± 9.9) years % male: 56.8%	NA	Mean $CHADS_2$ score: 1.9 (SD 1.2) Mean CHA_2DS_2-VAS_C score: 3.4 (SD 1.7)	NA
	Persistent AF: n/N=944/3667 (27%)		Mean age: 71.4 (± 9.1) years % male: 59.7%		Mean $CHADS_2$ score: 2.1 (SD 1.2) Mean CHA_2DS_2-VAS_C score: 3.7 (SD 1.6)	
	Permanent AF: n/N=1525/3667 (42%) (*non-specified in 6% patients*)		Mean age: 73.7 (± 8.4) years, p<0.0001 % male: 58.4%, p<0.0001		Mean $CHADS_2$ score: 2.4 (SD 1.3), p<0.0001 Mean CHA_2DS_2-VAS_C score: 4.1 (SD 1.7)), p<0.0001	
Steinberg 2015 [19] Subgroup *post hoc* analysis from RCT	Paroxysmal AF: n/N=2514/14062 (17.9%)	Patients experiencing episodic AF, self-terminating within 7 days, are said to have paroxysmal AF; patients whose arrhythmia persists beyond 7 days (or	Median age: 72 (25^{th}, 75^{th} percentile: 65, 78) years % male: 55%	**Stroke** Events/100 patient years (total events): 1.59 (78)	Mean $CHADS_2$ score: 3.5 (SD 0.9) Mean CHA_2DS_2-VAS_C score: 4.9 (SD 1.3)	**All-cause mortality** Events/100 patient years (total events): 3.52 (170)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
(*follow-up data were presented up to 30 months)*	Persistent AF: n/N=11548/14 062 (82.1%)	requires intervention to terminate) are considered to have persistent AF.	Median age: 73 (25^{th}, 75^{th} percentile: 65, 78) years, p=0.033 % male 61%, p<0.001	**Stroke** 2.02 (446) Adjusted HR: 0.78 (95% CI 0.61, 0.99), p=0.045	Mean $CHADS_2$ score: 3.5 (SD 0.9), p=0.32 Mean CHA_2DS_2-VAS_C score: 4.9 (SD 1.3), p=0.07	**All-cause mortality** 4.78 (1029) Adjusted HR: 0.79 (95% CI 0.67, 0.94), p=0.0061
Vanassche 2015 [20] (*subgroup analysis from two double-blind, placebo controlled RCTs*) *Data on follow-up NR*	Paroxysmal AF: n/N=1576/657 3 (24%)	Paroxysmal AF episodes are self-limiting and shorter than 1 week, episodes lasting longer than 7 days are referred to as persistent, and permanent AF refers to AF without any intercurring sinus rhythm.	Mean age: 69.0 (± 9.9) years % male: 52.3%	**Stroke** No, of events/patient: 77/1576 Event rate %/year: 2.1%	% Mean CHA_2DS_2-VAS_C score 2-3: 795 (50.5%) ≥4: 579 (36.8%)	NR by type of AF
	Persistent AF: n/N=1136/657 3 (17%)		Mean age: 68.6 (± 10.2) years % male: 57.7%	**Stroke** No, of events/patient: 74/1136 Event rate %/year: 3.0% Adjusted HR 1.44 (95% CI; 1.05, 1.98), p=0.02	Mean $CHADS_2$ score: 3.1 (SD 1.4) % Mean CHA_2DS_2-VAS_C score 2-3: 565 (49.7%) ≥4: 412 (36.3%)	
	Permanent AF: n/N=3854/657 3 (59%)		Mean age: 71.9 (± 9.8) years, p<0.001 % male: 60.2%, p<0.001	**Stroke** No, of events/patient: 385//3854 Event rate %/year: 4.2% Adjusted HR 1.83 (95% CI; 1.43, 2.35), p<0.001	Mean $CHADS_2$ score: 3.6 (SD 1.5), p<0.001 % Mean CHA_2DS_2-VAS_C score 2-3: 1677 (43.5%) ≥4: 1911 (49.6%), p<0.001	

AF: Atrial fibrillation; CI: Confidence interval; ECG: Electrocardiogram; HR: Hazard ratio; IQ: Interquartile range; NA: Not applicable; NIHSS: National Institutes of Health Stroke Scale; NR: Not reported; NVAF: Non-valvular atrial fibrillation; SD: Standard deviation; TE: Thromboembolism

Table 3.3. Studies relevant to criterion 1 (question 1b): study characteristics

Reference	Study design	Objective	Data source and country	Data collection	Population
Potpara 2013 [21]	Prospective cohort	To investigate baseline characteristics and long-term prognosis of carefully characterised asymptomatic and symptomatic patients with atrial fibrillation (AF) in a 'real-world' cohort of first-diagnosed non-valvular AF over a 10-year follow-up period.	Belgrade Atrial Fibrillation Study, in the Clinical Center of Serbia	Between 1992 and 2007 with a 10 year follow-up period	1,100 consecutive patients with first-diagnosed, non-valvular AF
Rienstra 2014 [22, 79]	Subgroup *post hoc* analysis from a RCT	To investigate potential differences in the clinical profile and prognosis of asymptomatic and symptomatic patients with recurrent persistent AF as included in the Rate Control versus Electrical cardioversion for persistent atrial fibrillation (RACE) study.	Data from the Rate Control versus Electrical cardioversion for persistent atrial fibrillation (RACE) study, The Netherlands	June 1998 to July 2001. Mean follow-up 2.3 ± 0.6 years	522 patients with AF

AF: Atrial fibrillation; ECG: Electrocardiogram

Table 3.4. Studies relevant to criterion 1 (question 1b): outcomes

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
Potpara 2013 [21] Prospective cohort (*baseline data and 10 years follow-up*)	Asymptomatic AF: n/N = 146/1100 (13.3%)	Asymptomatic AF was defined as AF documented by 12-lead ECG during regular visit, in the absence of any new symptoms (e.g. palpitations, tachycardia, fatigue, malaise, etc.) or worsening of pre-existent symptoms related to other illness. In patients without pre-existent medical conditions, AF was diagnosed accidentally during medical examination for other reasons (for example, annual examinations of employees, medical examination for driver's licence), and was labelled as first-diagnosed asymptomatic AF only if there was an evidence of sinus rhythm in the previous 12 months and the patient denied any recent change in the self-perception of his/her physical condition.	Mean age: 53.1 (± 13.1) years % male: 83.6%	Any stroke or systemic thromboembolic event: 17 (11.6%) Ischaemic stroke: 14 (9.6%)	% $CHADS_2$ score 1: 56 (38.4%) % $CHADS_2$ score ≥2: 21 (14.4%) % CHA_2DS_2-$VASc$ score 1: 42 (28.8%) % CHA_2DS_2-$VASc$ score ≥2: 48 (32.9%)	**Cardiovascular death** 8 (5.6%) **All cause death** 10 (6.8%)
	Symptomatic AF: n/N = 954/1100 (86.7%)		Mean age: 52.6 (± 12.1) years, p=0.61 % male: 61.7%, p<0.001	Any stroke or systemic thromboembolic event: 71 (7.4%) HR 1.6 (95% CI 1.0, 2.8), p=0.08 Ischaemic stroke: 44 (4.6%) HR 2.1 (95% CI 1.2, 3.9), p=0.02	% $CHADS_2$ score 1: 418 (43.8%), p=0.22 % $CHADS_2$ score ≥2: 96 (10.1%), p=0.12 % CHA_2DS_2-$VASc$ score 1: 333 (34.9%), p=0.15 % CHA_2DS_2-$VASc$ score ≥2: 348 (36.5%), p=0.40	**Cardiovascular death** 54 (5.8%) HR 0.9 (95% CI 0.4, 1.9), p=0.83 **All cause death** 75 (7.9%) HR 0.8 (95% CI 0.4, 1.6), p=0.61
Rienstra 2014 [22] Subgroup data from a RCT	Asymptomatic AF: n/N = 157/522 (30%)	Not reported	Mean age: 67 (± 9) years % male: 72%	NR	Mean $CHADS_2$ score: 1.2 (SD 1.1)	**Death from cardiovascular causes** 8 (5%)

Reference, study type and follow-up	Comparison (sample size)	Definition of AF clinical types	Patient characteristics	Stroke	Stroke risk	Stroke mortality
(mean follow-up 2.3 ± 0.6 years)	Symptomatic AF: n/N = 365/522 (70%)		Mean age: 69 (± 9) years, p=0.01 % male: 60%, p=0.007		Mean $CHADS_2$ score: 1.7 (SD 1.1), p<0.001	**Death from cardiovascular causes** 28 (8%) Absolute difference -2.6 (95% CI: -7.1, 2.0), p=0.27

AF: Atrial fibrillation; ECG: Electrocardiogram; NR: Not reported; SD: Standard deviation

Question 2

No studies met the eligibility criteria for this question.

Question 3

Table 3.5. Studies relevant to criterion 3: overview of studies

Study reference	Study design	Population	Index test and reference standard	Diagnostic performance outcomes
Systematic review				
Welton 2017 [26]	Systematic review with Prospective single-gate: 10 Two-gate: 2 Unclear design: 2	<u>Primary study location</u> Studies conducted in primary care: 4	<u>Index tests used in primary studies</u> The index test used was classified into one of eight categories to facilitate the analyses: • Pulse palpation	Summary results for each test using HSROC modelling <u>Modified blood pressure monitor (2 studies)</u> Sensitivity: 0.955 (0.864 to 0.992) Specificity: 0.919 (0.777 to 0.982)

	Studies conducted in outpatient, secondary or tertiary care services: 10 <u>Age</u> Age was an inclusion criterion in seven studies. Participants had to be ≥ 18 years in two studies, ≥ 35 years in one study, ≥ 60 years in one study, ≥ 65 years in two studies and ≥ 75 years in one study. <u>Prevalence of AF</u> Among the included studies, the prevalence of AF varied between 0.93% and 32.93%	• Photoplethysmography • Modified blood pressure monitor • Single-lead ECG ➢ 1- and < 12-lead ECG • 12-lead ECG • Ambulatory monitoring • Two-stage screening <u>Reference standard</u> All included studies 12-lead ECG interpreted by a cardiologist, apart from one study that used an ECG classified by a clinician and validated by a cardiac electrophysiologist.	DOR: 2.51 (2.17 to 2.67) <u>Single-lead ECG (5 studies)</u> Sensitivity: 0.961 (0.917 to 0.986) Specificity: 0.94 (0.882 to 0.976) DOR: 2.56 (2.42 to 2.65) <u>Two-stage screening strategy (7 studies)</u> Sensitivity: 0.943 (0.838 to 0.988) Specificity: 0.966 (0.9 to 0.992) DOR: 2.63 (2.46 to 2.7) <u>Photoplethysmography (1 study)</u> Sensitivity: 1 (1 to 1) Specificity: 0.867 (0.534 to 0.987) DOR: 2.39 (1.71 to 2.68) <u>12-lead ECG (7 studies)</u> Sensitivity: 0.927 (0.859 to 0.968) Specificity: 0.974 (0.95 to 0.989) DOR: 2.65 (2.59 to 2.69) <u>>1 and <12-lead ECG (2 studies)</u> Sensitivity: 0.839 (0.553 to 0.973) Specificity: 0.993 (0.978 to 0.999) DOR: 2.7 (2.66 to 2.72) <u>Pulse palpation (2 studies)</u> Sensitivity: 0.916 (0.75 to 0.986) Specificity: 0.788 (0.51 to 0.945) DOR: 2.21 (1.67 to 2.57)

Additional primary studies				
Hald 2017 [23]	Prospective single gate Consecutive patients visiting one of 49 primary care practices in Denmark were asked to participate. The patients entered in the opportunistic screening study were stratified into different age groups: 65–74 years, 75–84 years, and ≥85 years, respectively. The individual primary care practices were cluster randomised to one of the three age groups	n=970 Mean age: 75.1 (SD 7.1) Male: 44.7% Known AF: 0% Hypertension: 63.3% Diabetes: 20.1% IHD: 10.3% Heart failure: 3.8% Stroke or TIA: 6.1% COPD: 10.6% Valvular heart disease: 1.2% Peripheral arterial disease: 3.7% Medication affecting heart rhythm: NR	Index test: Pulse palpation. A clinic nurse measured the included patients radial pulse by palpation with the second, third and fourth fingers. The pulse beats were counted and interpreted by the nurse in a defined period, e.g. 30 or 60 seconds (rate per minute). Reference standard: 12-lead ECG An ECG recording was performed for all patients being detected with an irregular pulse. The ECG recordings were collected post study for blinded specialist examination performed by two skilled AF specialists. One specialist belonging to the study steering committee examined the ECG tracings as received from the investigators and in parallel a specialist from a Regional hospital examined printed copies. The two specialists were without knowledge on the ECG interpretations made by the GP investigators and were also blinded to one another	<u>Pulse palpation vs 12-lead ECG interpreted by a cardiologist</u> Detection rate: 1.03% (95%CI: 0.40, 1.67) PPV: 11.49% (calculated by YHEC) The detection rate was lower for 65-74 (0.83%) and 75-84 (0.54%) age groups than it was for the >85 age group (3.39%) <u>Pulse palpation vs 12-lead ECG interpreted by a GP</u> Detection rate: 1.34% (95%CI: 0.62, 2.06) PPV: 14.94% (calculated by YHEC) The detection rate was lower for 65-74 (1.04%) and 75-84 (1.08%) age groups than it was for the >85 age group (3.39%)
Kristensen 2016 [24]	Prospective single gate. The authors invited patients with and without known paroxysmal AF who came for an annual routine health check to	n=89 Mean age: 37 (Range 18-92) Male: 54% Known AF: 36% Hypertension:54%	Index test: portable three lead ECG monitor PEM The PEM was capable of storing the data/ECG. The ECGs were transferred from the PEM to a personal computer and were	Prevalence of AF using index test: 15.70% Prevalence of AF using reference standard: 16.90% Sensitivity: 68.67%

	be screened and one GP clinic in Denmark. The authors aimed to include 30–50% with a diagnosis of AF and 50–70% without AF.	Diabetes: 21% IHD: 11% Heart failure: NR Stroke or TIA: NR COPD: NR Valvular heart disease: NR Peripheral arterial disease: NR Medication affecting heart rhythm: 47%	evaluated by two trainee GPs after printing. Reference standard: 12-lead ECG interpreted by a senior GP or cardiologist	Specificity: 98.65% PPV: 92.86% NPV: 97.33% LR+: 64.13 LR-: 0.14 Accuracy: 96.63%
Svennberg 2017 [25](STROKESTOP)	Prospective single gate All residents of Stockholm county (n=23,888) or the rural region of Halland (n=4880) born in 1936 or 1937 were randomized to be invited by mail to participate in a screening programme for AF, or to enter a control group	n=7173 Mean age: Not reported, all >75 years Male: 46.3% Known AF: 9.3% Hypertension: 49.7% Diabetes:11.1% IHD: NR Heart failure: 3.4% Stroke or TIA: 9.0% COPD: NR Valvular heart disease: NR Peripheral arterial disease: 9.1% Medication affecting heart rhythm: NR	Index test: Hand-held one-lead device interpreted by an algorithm Participants were shown how to use a handheld one-lead device for intermittent ECG recordings during a 2-week period and instructed to register ECGs using their thumbs two times a day. The device had an integrated mobile transmitter that sent 30s ECG strip data to a database. An algorithm then sorted the ECGs into four categories: (0) poor quality, (1) only minor rhythm deviation or sinus rhythm, (2) irregular rhythm requiring manual interpretation (possible AF), and (3) other pathologies. Reference standard: Hand held one lead device interpreted manually. ECG recordings were manually interpreted by specially trained	Sensitivity: 97.84% Specificity: 88.20% PPV: 2.84% NPV: 99.99% LR+ 9.33 LR-: 0.02 Accuracy: 89.54%

						research nurses, and all abnormal ECGs were referred to the investigating cardiologist. When results were unclear, referral for interpretation by a consensus group was used.

COPD: Cardiopulmonary disease; ECG: Electrocardiogram; NR: Not reported; NPV: Negative predictive value; PPV: Positive predictive value; TIA: Transient ischaemic attack

Table 3.6. Studies relevant to criterion 3: study characteristics of the diagnostic accuracy studies (primary studies)

Reference	Study design	Objectives	Study sampling details	Date study data was collected	Index test(s)	Reference standard
Hald 2017 [23]	Prospective single-gate Opportunistic screening	To investigate the detection rate (undiscovered prevalence) of newly diagnosed AF patients among consecutively screened patients in routine daily clinical practice in Denmark.	Consecutive patients visiting one of 49 GP clinic in Denmark were asked to participate. The patients entered in the opportunistic screening study were stratified into different age groups: 65–74 years, 75–84 years, and ≥85 years, respectively. The individual primary care practices were cluster randomised to one of the three age groups.	January to March 2016	Pulse palpation. The clinic nurse measured the patients radial pulse by palpation with the second, third and fourth fingers. The pulse beats were counted and interpreted by the nurse ina defined period, e.g. 30 or 60 seconds (rate per minute).	12-lead ECG recording was performed for all patients being detected with an irregular pulse. The ECG recordings were collected post study for blinded specialist examination performed by two skilled AF specialists. One specialist belonging to the study steering committee examined the ECG tracings as received from the investigators and in parallel a specialist from a Regional hospital examined printed copies. The two specialists were without knowledge on the ECG interpretations made by the

						GP investigators and were also blinded to one another.
Kristensen 2016 [24]	Prospective single-gate Opportunistic screening	To evaluate how well an inexpensive portable three-lead ECG monitor PEM identified patients with atrial fibrillation (AF) compared to a normal 12-lead ECG.	The authors invited patients from one GP clinic in Denmark who either had known paroxysmal AF or were invited among patients who came for an annual routine health check. The authors aimed to include 30–50% with a diagnosis of AF and 50–70% without AF.	April 2014 to February 2015	A 30 s three-lead recording using a PEM device (Portable ECG Monitor, Beijing Choice Electronic Technology Co., Ltd., Beijing, China) The PEM was capable of storing the data/ECG. The ECGs were transferred from the PEM to a personal computer and were evaluated after printing.	12-lead ECG interpreted by a senior GP or cardiologist.
Svennberg 2017 (STROKESTOP) [25]	Prospective single-gate Population based screening	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.	All individuals born in 1936 or 1937 and living in Stockholm county (n = 23 888) or in the rural region of Halland (n = 4880) at the end of 2011 was randomized in a 1:1 fashion to be invited by mail to participate in a screening programme for AF, or to enter a control group.	April 2014 to February 2015	Handheld one-lead device (www.zenicor.com) for intermittent ECG recordings by participants during a 2-week period. Participants were instructed to register ECGs using their thumbs two times a day. The device had an integrated mobile transmitter that sends 30 s ECG strip data to a database. The AF was defined as at least one 30-s10 recording with irregular rhythm without p-waves, or a minimum of two similar episodes lasting 10–29 s during 2 weeks of intermittent recording.	Hand held one-lead device where ECG recordings were manually interpreted by specially trained research nurses, and all abnormal ECGs were referred to the investigating cardiologist. When results were unclear, referral for interpretation by a consensus group was used.

AF: Atrial fibrillation; ECG: Electrocardiogram; GP: General practitioner

Table 3.7. Studies relevant to criterion 3: participant characteristics of the diagnostic accuracy studies (primary studies)

Reference	N	Age	Gender	Known AF	Hpt	Diabetes	Ischaemic Heart disease	Heart failure	Stroke or TIA	COPD	Valvular heart disease	Peripheral arterial disease	Medication affecting heart rhythm
Hald 2017 [23]	970	Mean: 75.1 (SD 7.1)	Male: 434 (44.7%) Female: 536 (55.3%)	0 (0%)	614 (63.3%)	195 (20.1%)	100 (10.3%)	37 (3.8%)	59 (6.1%)	103 (10.6%)	12 (1.2%)	36 (3.7%)	NR
Kristensen 2016 [24]	89	Mean: 67 Range 18 to 92)	Male: 48 (54%) Female: 41 (46%)	32 (36%)	48 (54%)	19 (21%)	10 (11%)	NR	NR	NR	NR	NR	42 (47%)
Svennberg 2017[25]	7173	NR, all >75 years	Male: 3324 (46.3%) Female: 3849 (53.7%)	666 (9.3%)	3566 (49.7%)	794 (11.1%)	NR	247 (3.4%)	648 (9.0%)	NR	NR	664 (9.1%)	NR

AF: Atrial fibrillation; N: Number of participants; Hpt: Hypertension; COPD: Cardiopulmonary disease; NR: Not reported; SD: Standard deviation; TIA: Transient ischaemic attack

Table 3.8. Studies relevant to criterion 3: outcomes (screening performance) reported in the systematic review and primary studies

Trial reference	Screening test	N/n	Detectionrate	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Accuracy	DOR
Systematic review											
Welton 2017 [26]	Modified blood pressure monitor	2 studies	NR	0.955 (CrI 0.864 to 0.992)	0.919 (CrI 0.777 to 0.982)	NR	NR	NR	NR	NR	2.51 (CrI 2.17 to 2.67)
Welton 2017 [26]	Single lead ECG	5 studies	NR	0.961 (0.917 to 0.986)	0.94 (0.882 to 0.976)	NR	NR	NR	NR	NR	2.56 (2.42 to 2.65)
Welton 2017 [26]	Single lead ECG – Automatic/algorithm	3 studies	NR	0.967 (0.9 to 0.995)	0.9 (0.742 to 0.975)	NR	NR	NR	NR	NR	2.46 (2.1 to 2.65)
Welton 2017 [26]	Single lead ECG - nurse	1 study	NR	0.929 (0.711 to 0.995)	0.92 (0.7 to 0.992)	NR	NR	NR	NR	NR	2.52 (2.01 to 2.7)
Welton 2017 [26]	Single lead ECG – GP	1 study	NR	0.94 (0.671 to 0.999)	0.973 (0.838 to 1)	NR	NR	NR	NR	NR	2.65 (2.31 to 2.72)
Welton 2017 [26]	Single lead ECG – cardiologist	2 studies	NR	0.959 (0.878 to 0.992)	0.927 (0.802 to 0.984)	NR	NR	NR	NR	NR	2.53 (2.23 to 2.67)
Welton 2017 [26]	Two stage screening strategy	2 studies	NR	0.943 (0.838 to 0.988)	0.966 (0.9 to 0.992)	NR	NR	NR	NR	NR	2.63 (2.46 to 2.7)
Welton 2017 [26]	Photoplethysmography	1 study	NR	1 (1 to 1)	0.867 (0.534 to 0.987)	NR	NR	NR	NR	NR	2.39 (1.71 to 2.68)
Welton 2017 [26]	12-lead ECG	7 studies	NR	0.927 (0.859 to 0.968)	0.974 (0.95 to 0.989)	NR	NR	NR	NR	NR	2.65 (2.59 to 2.69)
Welton 2017 [26]	12-lead ECG – Automatic/algorithm	6 studies	NR	0.903 (0.803 to 0.961)	0.98 (0.958 to 0.993)	NR	NR	NR	NR	NR	2.67 (2.61 to 2.7)

Welton 2017 [26]	12-lead ECG – nurse	1 study	NR	0.967 (0.824, 1)	0.84 (0.484 to 0.982)	NR	NR	NR	NR	NR	2.33 (1.62 to 2.67)
Welton 2017 [26]	12-lead ECG – GP	1 study	NR	1 (1 to 1)	0.973 (0.843 to 1)	NR	NR	NR	NR	NR	2.65 (2.32 to 2.72)
Welton 2017 [26]	>1 and <12 lead ECG	2 studies	NR	0.839 (0.553 to 0.973)	0.993 (0.978 to 0.999)	NR	NR	NR	NR	NR	2.7 (2.66 to 2.72)
Welton 2017 [26]	>1 and <12 lead ECG – Automatic/algorithm	1 study	NR	0.83 (0.474 to 0.978)	0.985 (0.937 to 0.999)	NR	NR	NR	NR	NR	2.68 (2.55 to 2.71)
Welton 2017 [26]	<1 and <12 lead ECG – cardiologist	1 study	NR	0.981 (0.756 to 1)	1 (0.999 to 1)	NR	NR	NR	NR	NR	2.72 (2.72 to 2.72)
Welton 2017 [26]	Pulse palpation	2 studies	NR	0.916 (0.75 to 0.986)	0.788 (0.51 to 0.945)	NR	NR	NR	NR	NR	2.21 (1.67 to 2.57)
Primary studies											
Hald 2017 [23]	Pulse palpation interpreted by cardiologist – Total population (>65)	970	1.03(0.40,1.67)	NR	NR	11.49 %	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by cardiologist – 65-74 years	480	0.83(0.02,1.65)	NR	NR	19.05 %	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by cardiologist – 75-84 years	372	0.54(0.00,1.28)	NR	NR	5.13%	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by cardiologist - >85 years	118	3.39(0.12,6.66)	NR	NR	14.81 %	NR	NR	NR	NR	NR

Hald 2017 [23]	Pulse palpation interpreted by a GP – Total population (>65 years)	970	1.34%(0.62,2.06)	NR	NR	14.94%	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by a GP – 65-74 years	480	1.04%(0.13,1.95)	NR	NR	23.81%	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by a GP – 75-84 years	372	1.08%(0.03,2.12)	NR	NR	10.26%	NR	NR	NR	NR	NR
Hald 2017 [23]	Pulse palpation interpreted by a GP – >85 years	118	3.39%(0.12,6.66)	NR	NR	14.81%	NR	NR	NR	NR	NR
Kristensen 2016 [24]	PEM	89	NR	86.67%	98.65%	92.86%	97.33%	64.13	0.14	96.63%	NR
Svennberg 2017 [25]	12 lead ECG interpreted by algorithm	7173	NR	97.84%	88.20%	2.84%	99.99%	9.33	0.02	89.54%	NR

CrI: Credible interval; ECG: Electrocardiogram; GP: General practitioner; NR: Not reported

Question 4

Table 3.9. Studies relevant to criterion 4: study characteristics of the systematic reviews

Reference	Study design	Objective	Search dates	Population	Intervention and comparators	Outcomes	Included RCTs
Systematic reviews							
Moran 2013 [29]; 2015 [30]; 2016 [9]	Systematic review of RCTs	The primary objective of the primary and updated reviews by Moran were to investigate whether evidence shows differences between systematic screening and routine practice in the detection of new cases of AF. The secondary objectives were to identify which combination of	Up to Mar and June 2012 (Moran 2013) [29]; Updated searches: Up to June 2012 to June 2015 (Moran 2015)[80] Nov to Dec 2015 (Moran	Men and women over the age of 40 years	Population-based, targeted or opportunistic screening programmes versus no screening, in which the control group relied on routine practice for the diagnosis of AF over the relevant time period.	**Primary**: the difference in the detection of new cases of AF **Secondary:** acceptability of systematic screening programmes within the target population; adverse events associated with	1. Hobbs et al. 2005[63]********** (SAFE) (included in Moran 2013 [29]; 2015[30]; 2016[9]) 2. Svennberg et al. 2005 [59]†††††††††††† E (STROKESTOP) (included in Moran 2015) 3. Perula-de-Torres et al. 2012 [81]‡‡‡‡‡‡‡‡‡‡‡‡ (DOFA-AP) (included in Moran 2015[30])

********** Hobbs FDR, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess. 2005; 9(40) p.iii-71.

†††††††††††† Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study. Circulation. 2015 131:2176–84.

‡‡‡‡‡‡‡‡‡‡‡‡ Perula-de-Torres LA, Martinez-Adell MA, Gonzalez-Blanco V, Baena-Diez JM, Martin-Rioboo E, Parras-Rejano JM, et al. Opportunistic detection of atrial fibrillation in subjects aged 65 years or older in primary care: a randomised clinical trial of efficacy. DOFA-AP study protocol. BMC Family Practice. 2012;13:106.

Reference	Study design	Objective	Search dates	Population	Intervention and comparators	Outcomes	Included RCTs
		screening strategy and patient population is most effective, as well as assessing any safety issues associated with screening, its acceptability within the target population and the costs involved.	2016)[9, 30, 61]			systematic screening programmes for AF; analysis of costs associated with systematic screening programmes for AF; changes to the known prevalence of AF	
Welton 2017[82]	Systematic review of RCTs	The objective of this systematic review was to update the Cochrane review of screening strategies for AF (Moran above).	Up to July 2015 to Dec 2015	Adults aged ≥ 40 years of either sex	Screening strategies, defined by screening test, age at initial and final screens, screening interval and format of screening	**Primary**: the difference in the detection of new AF cases associated with screening compared with usual practice. **Secondary:**	1. Hobbs et al. 2005 [63]; Fitzmaurice et al. 2014 [71] §§§§§§§§§§§ (SAFE) 2. Friberg et al. 2013 [83] **********; Svennberg et al. 2005 [59](STROKESTOP)

§§§§§§§§§§§ Fitzmaurice DA, Hobbs FD, Jowett S, Mant J, Murray ET, Holder R, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. BMJ 2007;335:383.

********** Friberg L, Engdahl J, Frykman V, Svennberg E, Levin LÅ, Rosenqvist M. Population screening of 75- and 76-year-old men and women for silent atrial fibrillation (STROKESTOP). Europace 2013;15:135–40.

Reference	Study design	Objective	Search dates	Population	Intervention and comparators	Outcomes	Included RCTs
					(systematic opportunistic screening [individuals offered screening if they consult with their general practitioner (GP)] or systematic population screening (when all eligible individuals are invited to screening)).	1. change in diagnosed AF (after screening compared with before screening); 2. the acceptability of systematic screening programmes 3. adverse events associated with systematic screening 4. costs associated with systematic screening programmes for AF.	3. Perula-de-Torres et al. 2012 (DOFA-AP) [81] 4. Morgan and Mant (no trial name) 2002 [84]†††††††††††† 5. Benito et al. 2013[62]‡‡‡‡‡‡‡‡‡‡‡‡ (EARLY)

AF: Atrial fibrillation; RCT: Randomised controlled trial

†††††††††††† Morgan S, Mant D. Randomised trial of two approaches to screening for atrial fibrillation in UK general practice. Br J Gen Pract 2002;52:373–4, 377–80.

‡‡‡‡‡‡‡‡‡‡‡‡ Benito L, Coll-Vinent B, Gómez E, Martí D, Mitjavila J, Torres F, et al. EARLY: a pilot study on early diagnosis of atrial fibrillation in a primary healthcare centre. Europace 2015;17:1688–93.

Table 3.10. Studies relevant to criterion 4: study outcomes as reported in the systematic reviews of RCTs

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
Moran 2013[29]; 2015[30]; 2016[9]	1. Hobbs et al. 2005 [63][52] (SAFE) (included in Moran 2013[29]; 2015[30]; 2016[9]) (n=15,000 randomised)	Systematic screening: patients over 65 years of age received a letter inviting them to attend an electrocardiogram (ECG) screening clinic	1. Opportunistic screening: patients' records were flagged to prompt the general practitioner (GP) to check the pulse whenever that patient next attended the practice for any reason 2. Routine care comparator (no screening)	12 months	The authors stated "*No specific **adverse events** associated with screening were reported. **Anxiety** levels and **quality of life** were measured at baseline and at the end of the study with the six-item Spielberger State Anxiety Inventory and the five-item EQ-5D. A total of 777 post-screening questionnaires were distributed, and 630 were returned, 535 of which were completed: 479 participants completed the six-item Spielberger State Anxiety Inventory, and 520 competed the five-item EQ-5D.No significant difference was found between the two intervention arms at the end of the study for anxiety (z = -1.699, P value = 0.089) or quality of life (z = -1.166, P value = 0.244).*" (Moran 2016)	The authors stated "*The risk of bias in the SAFE study is low. Blinding of participants was not possible given the nature of the intervention, but the clinicians who read the ECGs were blinded as to which group the tracing came from.*" (Moran 2015 [30])

[52] Hobbs FDR, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. Health Technol Assess. 2005; 9(40) p.iii-71.

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
	2. Svennberg et al. 2005 [59][53] E (STROKESTOP) (only included in Moran 2015[30]) (n= 14,387)	AF screening programme where patients were given handheld one-lead ECG recorders	Standard of care (no screening)	This publication is not relevant to this NSC review as relevant outcomes for the NSC review were not reported		
	3. Perula-de-Torres et al. 2012 [81][54] (DOFA-AP) (only included in Moran 2015)	Opportunistic screening of over 65s in primary care	Routine care (no screening)	This study was a protocol and no outcomes were reported		
Welton 2017 [26]}	1. Hobbs et al. 2005 [63]; Fitzmaurice et al. 2014 [71][55] (SAFE) (n=14,802)	Systematic population screening of individuals ≥ 65 years: 12 lead interpreted by a cardiologist	1. Systematic opportunistic of individuals ≥ 65 years: pulse palpation by a GP or nurse followed by 12-lead ECG interpreted by a cardiologist if pulse irregular	12 months	The authors reported "*A random sample of individuals randomised to the screening arms of the trial was sent the postal version of the EuroQol-5 Dimensions (EQ-5D) (to measure **quality of life**) and the shortened Spielberger anxiety*	The authors reported "*The SAFE study…was a well-conducted study at low risk of bias on all domains except blinding of participants/personnel (which is not possible) and*

[53] Svennberg E, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Mass Screening for Untreated Atrial Fibrillation: The STROKESTOP Study. Circulation. 2015 131:2176–84.

[54] Perula-de-Torres LA, Martinez-Adell MA, Gonzalez-Blanco V, Baena-Diez JM, Martin-Rioboo E, Parras-Rejano JM, et al. Opportunistic detection of atrial fibrillation in subjects aged 65 years or older in primary care: a randomised clinical trial of efficacy. DOFA-AP study protocol. BMC Family Practice. 2012;13:106.

[55] Fitzmaurice DA, Hobbs FD, Jowett S, Mant J, Murray ET, Holder R, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. BMJ 2007;335:383.

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
			2. No screening (usual practice)		*questionnaire on study entry and again at the end of the screening period (approximately 17 months later), when it was also sent to all participants who had screened positive. In addition, all participants were asked to complete the Spielberger anxiety questionnaire immediately after screening. The EQ-5D scores were similar across the systematic population screening and systematic opportunistic screening arms at baseline and also at 12 months' follow-up. Similar results were found for* ***anxiety*** *scores."*	*blinding of outcome assessment (unclear risk of bias). One issue with the SAFE study was that the baseline prevalence of AF was slightly higher in the control group than in the screening group. This could potentially introduce bias because, if more AF cases were previously diagnosed in the control practices, there may be fewer cases that could be diagnosed subsequently through screening or routine care. This was explored in the SAFE study using an individual participant analysis controlling for differences in baseline prevalence, which showed that the conclusions of the SAFE study were robust to*

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
						adjustments to baseline prevalence."
	2. Friberg et al. 2013 [83][56]; Svennberg et al. 2005 [59] (STROKESTOP) (n=28,768)	Systematic population screening	No screening	Relevant outcomes for this NSC review were not reported		
	3. Perula-de-Torres et al. 2012 [81] (DOFA-AP)	Systematic opportunistic screening of individuals ≥ 65 years: Pulse palpitation by a GP	No screening	This study was a protocol and no outcomes were reported		
	4. Morgan and Mant (no trial name) 2002 [84][57] (n=3,001)	Systematic population screening of individuals ≥ 65 years: Pulse palpation by a	Systematic opportunistic screening: Pulse palpitation, with ECG validation at the discretion of	Relevant outcomes for this NSC review were not reported		

[56] Friberg L, Engdahl J, Frykman V, Svennberg E, Levin LÅ, Rosenqvist M. Population screening of 75- and 76-year-old men and women for silent atrial fibrillation (STROKESTOP). Europace 2013;15:135–40.
[57] Morgan S, Mant D. Randomised trial of two approaches to screening for atrial fibrillation in UK general practice. Br J Gen Pract 2002;52:373–4, 377–80.

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
		GP or a trained nurse, validated by two-lead ECG reading by a GP	nurse or GP taking the pulse			
	5. Benito et al. 2013 [62][58] (EARLY) (n=4,000)	Targeted screening of individuals ≥ 65 years: ECG, physical examination and medical history every 6 months	No screening	2 years	While secondary outcomes of this study included "complications related to AF (heart failure, stroke or systemic embolism, symptomatic bradycardia requiring pacemaker, and severe haemodynamic angina) or to its treatment (malignant arrhythmia or symptomatic bradycardia requiring pacemaker in patients on antiarrhythmic treatment, bleeding in patients on anticoagulant therapy)", the systematic review authors did not address these outcomes. Benito et al. was checked and the study authors reported that "*In the control group, one patient was diagnosed by a private cardiologist when consulting for chest pain, four patients were diagnosed incidentally in the*	It appears that this study was considered to be at high risk of bias by the review authors. They stated "*Many individuals were excluded from each arm for different reasons...Although the study reported that an intention-to-treat analysis was performed, it considered only the individuals included in the study. In the intervention group, individuals could decline to participate, but in the control group they could not. The study actually*

[58] Benito L, Coll-Vinent B, Gómez E, Martí D, Mitjavila J, Torres F, et al. EARLY: a pilot study on early diagnosis of atrial fibrillation in a primary healthcare centre. Europace 2015;17:1688–93.

Reference	Study and sample size (included the SR)	Intervention	Comparator	Duration	Results	Quality assessment by review authors
					hospital, and another in the emergency room due to a complication of AF (heart failure)… At the end of follow-up, no other patient had developed complications associated with the diagnosis of AF. All intervention group patients but one (with a CHA2DS2-VASc score of 0) were started on anticoagulation therapy, as were two patients in the CG. Two patients had developed mild complications related to treatment: one IG patient had cutaneous haematomas related to anticoagulation, and one CG patient developed bradycardia associated with amiodarone. Seven intervention group patients (1.5%) and 8 control group patients (1.7%) died during the study period."	*compared the incidence of AF in all people eligible for screening but who received usual care with the incidence of AF in a self-selecting subgroup of people who both were eligible and attended screening. On the basis of these methodological limitations, we felt that it was inappropriate to include the results from this study in our statistical analysis*."

AF: Atrial fibrillation; CG: Control group; ECG: Electrocardiogram; GP: General practitioner; IG: Intervention group; RCT: Randomised controlled trial

Table 3.11. Studies relevant to criterion 4: study characteristics of randomised controlled trials

Reference	Study design	Objective	Inclusion/ exclusion criteria	Intervention	Comparator	Duration	Outcomes
González Blanco 2017 [27]	Cluster RCT	To assess the effectiveness of opportunistic screening through pulse palpation in the early detection of AF in subjects aged >65 years versus detection through an active search for patients with symptoms and/or complications and sequelae associated with AF.	General practitioners and nurses from the Spanish National Health System were invited to participate in the study. Criteria for inclusion in the study consisted of being aged ≥65 years, attending the health center for other health problems and giving informed consent. Patients with a previous diagnosis of AF were excluded.	Opportunistic screening for AF through pulse palpation was performed on all patients seen by participating healthcare professionals, regardless of the reason for the visit. An ECG was performed on patients found to have an irregular heartbeat to confirm the diagnosis of auricular fibrillation (n=166 physicians and nurses, and 5,465 patients).	Screening was performed on any patient having symptoms suggestive of AF (general discomfort, dyspnea, chest pain, palpitations, dizziness, decreased resistance to physical activity), complications or sequelae potentially attributable to AF (stroke and TIA). An ECG was performed on patients found to have an irregular heartbeat to confirm the diagnosis of auricular fibrillation (n=182 physicians and nurses, and 1,525 patients).	24 months	**Primary:** Proportion of new cases of AF detected. **Secondary:** not explicitly reported, but the authors presented data on 'other electrocardiographic alterations' in the results section.
Halcox 2017 [28]	RCT	To assess twice-weekly monitoring with	Individuals >65 years of age with a CHADS-VASc score ≥2	Participants were instructed to undertake twice-weekly 30-second single lead iECG trace	Routine care; followed up as normal by a GP (n=501).	1 year	**Primary:** Time to diagnosis of AF

Reference	Study design	Objective	Inclusion/ exclusion criteria	Intervention	Comparator	Duration	Outcomes
REHEARSE-AF Study		the AliveCor Kardia device Versus routine clinical care in patients ≥65 years of age with ≥1 additional stroke risk factor on time to diagnosis of AF.	not in receipt of OAC therapy without a known diagnosis of AF currently, a known contraindication to anticoagulation, or permanent cardiac pacing implantation.	using the AliveCor Kardia device (a smartphone/tablet–based single-lead electrocardiographic capture system). iECG traces were analysed by an automated analysis software algorithm and sent for off-line analysis by a physiologist-led electrocardiographic reading service. Abnormal ECGs were read by a cardiologist (n=500).			**Secondary**: Adverse events (identified at the time of event or identified by telephone at 12, 32, and 52 week assessments).

AF: Atrial fibrillation; iECG: ipod electrocardiogram; OAC: Oral anticoagulant

Table 3.12. Studies relevant to criterion 4: outcomes of randomised controlled trials

Reference, study type and follow-up	Intervention and comparator	Patient characteristics	Results
González Blanco 2017 [27] (2 years)	Opportunistic screening for AF through pulse palpation was performed on all patients seen by participating healthcare professionals, regardless of the reason for the visit (n=5,465 patients) Screening was performed on any patient having symptoms suggestive of AF (n=1,525 patients)	Mean age: 74.1 (SD 6.6) years % male: 42% Obesity: 871 (16%) Arterial hypertension: 3543 (65%) Diabetes mellitus: 1530 (28%) Dyslipidaemia: 2431 (45%) Ischaemic heart disease: 396 (7%) PAD: 87 (2%) Stroke/TIA: 218 (4%) Valvular: 102 (2%) Left ventricular hypertrophy: 57 (1%) Heart failure: 80 (2%) Mean age: 75.6 (SD 7.2) years % male: 41% Obesity: 294 (19%) Arterial hypertension: 1054 (69%) Diabetes mellitus: 437 (29%) Dyslipidaemia: 635 (42%) Ischaemic heart disease: 150 (10%) PAD: 33 (2%) Stroke/TIA: 69 (5%) Valvular: 41 (3%) Left ventricular hypertrophy: 17 (1%) Heart failure: 35 (2%)	A total of 164 new cases of AF (2.34%) were detected, of which 61 were experimental patients (1.1%) and 103 were control group patients (6.8%) (RR 0.16 (95% CI: 0.11, 0.21); ARR 5.70% (95%CI: 4.77, 6.49%) in favour of the control group. Other electrocardiographic alterations were detected in 4.4% of patients (2.8% in the experimental group vs 10.0% in the control group): RR 0.20 (95% CI: 0.16, 0.25); ARR 9.0% (95% CI: 8.0, 11.0%).
Halcox 2017 [28] (REHEARSE-AF Study)	Twice-weekly monitoring with the AliveCor Kardia device (n=500)	Mean age: 72.6 (SD 5.4) years % male: 48% Heart failure: 5 (1%) Hypertension: 268 (54%) Diabetes mellitus: 129 (26%) Stroke or TIA: 35 (7%) Vascular disease: 71 (14%)	19 patients in the iECG group were diagnosed with AF during the 12-month study period versus 5 in the routine care arm (HR 3.9; 95% CI 1.4, 10.4) p=0.007. **Stroke risk (at diagnosis)** The iECG patients diagnosed with AF had CHADSVASc scores of 2 (n=3), 3 (n=5), 4 (n=7), 5 (n=2), and 6 (n=1);

Reference, study type and follow-up	Intervention and comparator	Patient characteristics	Results
RCT (1 year)	Routine care (n=501	Mean CHADS-VASc score: 3.0 (SD 1.0) Mean age: 72.6 (SD 5.4) years % male: 45% Heart failure: 9 (2%) Hypertension: 272 (55%) Diabetes mellitus: 140 (28%) Stroke or TIA: 28 (6%) Vascular disease: 79 (16%) Mean CHADS-VASc score: 3.0 (SD 1.0)	routine care patients with AF had CHADS-VASc scores of 2 (n=1), 3 (n=2), and 4 (n=2) (no statistical comparison reported). **Stroke/TIA/SE** There was no statistically significant difference between the groups (6 versus 10 in the iECG and routine care arms, respectively: HR 0.61 (95% CI 0.22, 1.69), p=0.34. **Adverse events** The authors stated that there were no significant differences in the number of serious adverse clinical events occurring in each arm (iECG vs. routine care): Death: 3 vs. 5, p=0.51 Clinically significant bleeds: 2 vs. 1, p=0.56 DVT/PE: 3 vs. 1, p=0.31 Other cardiovascular: 8 vs. 13, p=0.27 Respiratory: 7 vs. 3, p=0.20 Other neurological: 2 vs. 2, p=0.65 Orthopaedic/musculoskeletal/fall: 14 vs. 14, p=0.99 Gastroenterological: 10 vs. 10, p=0.99 Renal/urologic: 2 vs. 5, p=0.26 Other: 7 vs. 6, p=0.78

AF: Atrial fibrillation; ARR: Absolute risk reduction; CI: Confidence interval; DVT: Deep vein thrombosis; HR: Hazard ratio; iECG: ipod electrocardiogram; PAD: Peripheral artery disease; PE: Pulmonary embolism; RR: Relative risk; SE: Systemic embolism; TIA: Transient ischaemic attack

Question 5

Table 3.13. Studies relevant to criterion 5: study characteristics and outcomes of cost-effectiveness studies

Reference	Model structure	Screening strategies considered	Screening schedules (years)	Summary of cost effectiveness results	Study conclusion
Welton 2017 [26]	The analysis was based on a model consisting of a decision tree for the screening process and outcome and a discrete-time Markov model for treatment	Population-based, systematic (opportunistic, targeted or population) screening programmes for AF, including a 12 lead ECG, single-lead ECGs, between 1 and 12 lead ECGs, pulse palpation, modified blood pressure monitors, photoplethysmography and two-stage testing.	Single screening strategy at 50, 55, 60, 65, 70, 75 or 80 years. Repeat screening every five years starting at the ages above.	Single opportunistic screening was found to be cost-effective at £20,000 a QALY regardless of screen age and diagnostic methods. Opportunistic screening with photoplethysmography was found to have an ICER of £8065/QALY with screening at age 65 years. Repeat screening was also found to be cost-effective with the most cost-effective repeat strategy likely to be starting at age 65 years with five yearly intervals to age 80 years.	A national screening programme for AF was likely to represent a cost-effective use of resources. Systematic opportunistic screening was more likely to be cost-effective than systematic population screening.

AF: Atrial fibrillation; ECG: Electrocardiogram; ICER: Incremental cost-effectiveness ratio; QALY: Quality-adjusted life-year

Question 6

Table 3.14. Studies relevant to criterion 6a: study characteristics and outcomes

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
Das 2015 [31]	Observational cohort	To determine the outcome of a Primary Care AF (PCAF) service on anticoagulation uptake in a cohort of high-risk patients ($CHA2DS_2$-VASc ≥1) with AF in the UK.	UK – GRASP-AF	June 2012 to June 2014	Patients with AF who were eligible for but not taking anticoagulation (or taking warfarin but with a low time-in-therapeutic range) from 56 general practices in the UK (n=1063).	Of 1063 patients who were eligible for but not taking anticoagulation (or taking warfarin but with a low time-in-therapeutic range) 1020 (96%) agreed to start anticoagulation following a consultation. The remaining 16 (1.5%) patients declined treatment and a further 27 (2.5%) deferred their decision pending further discussion with their GP. **Compliance** 8 random practices were audited after 195 (185-606) days. 78/87 (90%) of patients who had started on a new anticoagulant therapy continued treatment (either on the initial agent or an alternative).
Hodgkinson 2011 [32]	Retrospective cohort	To explore the pattern of treatment pathways – i.e. how patients are treated over time – for patients with AF, and to test the hypothesis that comparative to patients in lower stroke-risk categories	UK – data from General Practice Research Database (GPRD)	Mostly from 1990 onwards	Patients with a diagnosis of AF from practices registered with the GPRD (n=67,857).	The authors reported that the average percentage of time patients with newly diagnosed AF remained on their original treatment with anticoagulants was 60.6% over the first year, and 27.3% over 5 years. The authors also reported that $CHADS_2$ scores did not correlate with likelihood of treatment continuation.

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
		(as measured by $CHADS_2$ score), patients with higher $CHADS_2$ scores are less likely to discontinue anticoagulant therapy or, if not started on anticoagulant treatment, more likely to be transferred to anticoagulant therapy, in keeping with guideline recommendation.				
Johnson 2016 [33]	Observational cohort	To examine the characteristics and persistence in patients newly initiated with oral anticoagulants (OACs) for stroke prevention in	UK Clinical Practice Research Datalink (CPRD)	December 2012 to October 2014	Patients with NVAF newly prescribed anticoagulants during routine clinical practice who were OAC naïve (n=13,089).	**Persistence** Of the 13,089 OAC naïve patients, persistence was assessed for 11,657 patients (89.1%) (9303 VKA, 1275 rivaroxaban, 656 dabigatran and 413 apixaban) who had a sufficient amount of follow-up. The authors stated that the pattern of persistence changed over the course of treatment. At 3 months' follow-up, persistence was high across all OAC

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
		non-valvular atrial fibrillation (NVAF).				cohorts ranging from 84.1% in dabigatran users to 93.4% in VKA users. At 6 months, the pattern changed with apixaban users having the highest rate of persistence (apixaban 88.2%; VKA 87.0%; rivaroxaban 80.7%; dabigatran 74.2%). Persistence remained highest with apixaban at 12 months (82.8%) followed by VKA (77.8%), rivaroxaban (73.1%) and was the poorest in dabigatran users (66.7%). However, it should be noted that the number of patients assessed at 12 months was particularly low in the apixaban cohort (n=70) compared to the other OACs (rivaroxaban n=493, dabigatran n=377, VKA n=4979). Overall persistence at the end of follow-up was 70.6% (95% CI 68.9% to 72.3%) among VKA patients, 62.5% (95% CI 57.5% to 67.6%) among dabigatran, 67.6% (95% CI 62.9% to 72.2%) among rivaroxaban and 82.8% (95% CI 76.8% to 87.9%) among apixaban patients.
Martinez 2016 [34]	Observational cohort	To compare persistence of non-VKA OAC (NOAC) with VKA treatment in the first year after OAC inception for incident AF in realworld practice.	UK Clinical Practice Research Datalink (CPRD)	January 2011 to May 2014	Patients with incident NVAF who were OAC naïve (n=27,514).	**Persistence** Of the patients taking NOACs (n=914), persistence at 90 days was 94.7%, 85.9% at 180 days, 82.4% at 270 days and 79.2% at 365 days. Of the patients taking VKAs (n=12,307), persistence at 90 days was 87.2%, 76.5% at 180 days, 69.3% at 270 days and 63.6% at 365 days. Differences between

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
						treatment groups at all time periods were statistically significant (p<0.001 for all). *Data are also presented for patients with CHA_2DS_2 VASC score <2 and ≥2 but have not been extracted.*
Mueller 2017 [35]	Retrospective cohort	To report the use of direct oral anticoagulants (DOACs) for stroke prevention in patients with atrial fibrillation in Scotland and advocate the standardisation of drug utilisation research methods.	Scotland – linked administrative data from PIS and SMR01	September 2011 to June 2014	Patients included those diagnosed with AF (confirmed in hospital) who received a first prescription for a DOAC (dabigatran, rivaroxaban, or apixaban) (n= 5398 patients with a mean $CHA2DS_2$ VASc score 2.98 [SD 1.71]).	Patients were treated with DOACs for a median of 228 days (interquartile range 105-425). **Discontinuation** The authors stated that 1923 patients (35.6%) discontinued treatment during the study period. Of these 11.0% switched to warfarin, and 48.3% reinitiated DOACs at least temporarily. By study conclusion, 1186 patients had stopped receiving DOAC prescriptions, resulting in a cessation rate of 22.0%; this figure includes patients ceasing all oral anticoagulant treatment as well as those switching lastingly to a VKA. **Persistence** Crude persistence with DOAC treatment regardless of switches between individual drugs was 82.1%, 75.9%, and 69.8% at 6, 12 and 18 months, respectively. **Adherence** Adherence to treatment with all DOACs was good: Overall DOAC median medication refill adherence was 102.9% (interquartile range 88.9%-115.5%), and

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
						82.3% of patients had a medication refill adherence > 80%. *Differences between individual DOACs were observed but this information has not been extracted.*

AF: Atrial fibrillation; DOAC: Direct oral anticoagulant; NOAC: Novel anticoagulants; NVAF: Non-valvular atrial fibrillation; OAC: Oral anticoagulant; PIS: Prescribing Information System; VKA: Vitamin K antagonists

Table 3.15. Studies relevant to criterion 6b: study characteristics and outcomes

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
Das 2015 [31]	Observational cohort	To determine the outcome of a Primary Care AF (PCAF) service on anticoagulation uptake in a cohort of high-risk patients ($CHA2DS_2$-VASc ≥1) with AF in the UK.	UK	June 2012 to June 2014	Patients with AF taking anticoagulation from 56 general practices in the UK (n=5471).	The authors stated that with the intervention of the PCAF service, the proportion receiving anticoagulation improved from 77% (4187/5471) to 95% (5207/5471) (p<0.0001).

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
Induruwa 2017 [37]	Prospective screening study	To investigate whether active screening for atrial fibrillation in secondary care, followed by careful evaluation of risk factors and communication to general practitioners from stroke specialists, could increase appropriate anticoagulation prescription.	Cambridge, UK	September 2014 and February 2015	Patients with AF in a secondary setting (n=847).	671 (79.2%) had an existing diagnosis of AF at admission, and of these 56% were on anticoagulation treatment. Of 145 patients newly diagnosed with AF on admission, 61 (42%) were started OAC on discharge.
Isaew 2017 [38]	Observational cohort -16 sequential cross-sectional analyses	To determine whether patients with paroxysmal AF are less likely to be treated with anticoagulants than patients with persistent or permanent AF in the UK and to investigate trends in treatment	UK – Data from The Health Improvement Network (THIN)	May 2000 to May 2015	Patients with AF from 648 practices (n=179,343)	The authors reported "Over the 15-year period studied, the proportion of patients with paroxysmal AF prescribed anticoagulants increased from 16.0% (95% CI 14.0 to 18.2) to 50.7% (95% CI 49.6 to 51.8), while the proportion of patients with other AF [persistent or permanent AF] prescribed anticoagulants increased from 33.5% (95% CI 32.7 to 34.3) to 67.1% (95% CI 66.6 to 67.5). Among eligible patients only, defined as those with a CHADS2 score of 1 or more, the proportion of patients with paroxysmal AF prescribed anticoagulants increased from 18.8% (95% CI 16.4 to 21.4) to 56.2% (95% CI 55.0 to 57.3), and the proportion of patients with other AF

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
		between 2000 and 2015.				prescribed anticoagulants increased from 34.2% (95% CI 33.3 to 35.0) to 69.4% (95% CI 68.9 to 69.8)."
Lonsdale 2016 [41]	Intervention study (involving education of prescribers and patient campaign of AF awareness) with GRASP data reported at different time periods to see if there was an effect	To implement the new NICE guidelines (CG180) by offering anticoagulants to people at highest risk of stroke, stopping aspirin monotherapy prescribed solely for AF, updating and enhancing patient registers for AF and investigating why patients may be out of	Fylde and Wyre, UK – Data (GRASP-AF) were taken at start of project and throughout implementation.	February 2015 to April 2016	Patients with AF at high risk (CHA_2DS_2 VASC score and ≥2) (the authors stated that the numbers increased from 3432 to 3754 throughout the time of the project)	In February 2015, the percentage of patients with CHA_2DS_2 VASC score ≥2 taking OACs appears to be 65.4% (*calculated based on data presented in the report [i.e. '2246 taking OACs in Feb 2015'] but the authors report a percentage of approximately 25% in a graph and it is not clear how this was derived*), and in April 2016 the percentage was 71.4% (n=2681).

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
		range for Time in Treatment (TTR).				
Martinez 2016 [34]	Observational cohort	To compare persistence of non-VKA OAC (NOAC) with VKA treatment in the first year after OAC inception for incident AF in real-world practice.	UK – Data from Clinical Practice Research Datalink (CPRD)	January 2011 to May 2014	Patients with incident NVAF who were OAC naïve (n=27,514).	The authors reported the percentage of new AF patients (with $CHA2DS_2$-VASc ≥2) treated with OACs changed from 41.2% in January 2011 to 65.5% in May 2014 (no statistical comparisons were reported).
Mazurek 2017 [42]	Observational cohort	To assess clinical outcomes of AF patients with versus without	Darlington, UK	March 2013	AF patients from 11 general practices in the UK (n=2259).	971 (43.0%) patients were prescribed OAC treatment, and 109 (4.8%) were prescribed OAC plus anti-platelets (367 [16.2%] did not receive any therapy and 812 [35.9%] received anti-platelets alone).

Reference	Study design	Objective	Region/data source	Data collection	Population	Results
		previous stroke in relation to guideline-adherent antithrombotic treatment for stroke prevention.				The authors also reported that “only approximately half [50.8%] of the eligible patients with AF are prescribed oral anticoagulation in line with [NICE] guidelines.”

AF: Atrial fibrillation; DOAC: Direct oral anticoagulant; OAC: Oral anticoagulant; VKA: Vitamin K antagonists

Appraisal for quality and risk of bias

Quality assessments of included studies are reported by question below.

Question 1

Table 3.16: Question 1a: Detailed risk of bias for RCTs (Cochrane) *with relevant subgroup analysis*

	Studies				
As reported in the publication[59]	**Al-Khatib 2013 [10]**	**Disertori 2013 [13]**	**Flaker 2012 [14]**	**Steinberg 2015 [19]**	**Vanassche 2015 [20]**
Was the allocation sequence adequately generated?	Unclear: Reportedly stratified for site and prior warfarin use, but actual method not reported.	Low: Central interactive automated telephone system	Low: central, interactive, automated telephone system.	Low risk: central, interactive, automated telephone system.	Low risk: central, interactive, automated telephone system.
Was allocation adequately concealed?	Low risk: Identical appearance of study drug and packaging	Low risk: central, interactive, automated telephone system.	Low risk: central, interactive, automated telephone system.	Low risk: central, interactive, automated telephone system.	Low risk: central, interactive, automated telephone system.
Were the care providers and/or participants blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	Low risk: Participants and investigators, did not have access to individual subject treatment assignments.	Low risk: Described as double-blind.	Unclear risk: Patients receiving dabigatran were blinded, people who were receiving warfarin were not.	Low risk: Described as double-blind.	Low risk: Described as double-blind.

[59] Full details of trial methodology were not often reported in these publications of subgroup analyses, but are likely reported elsewhere.

Were the outcome assessors blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	Low risk: Outcome assessors blinded	Unclear risk: not reported	Low risk: outcome assessors were blinded	Unclear risk: Not reported	Unclear risk: not reported
Incomplete outcome data - Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	Low risk: Of 18,201 participants, 74 were lost to follow up.	Low risk: Survival data was available for all included patients and first recurrence of AF was reported for 95.5% of patients.	Low risk: Of 18113 participants, 20 were lost to follow up. Rates of discontinuation were balanced across groups	Unclear risk: 93 patients were excluded from the efficacy analyses due to violations of Good Clinical Practice at the enrolling centre.	Unclear risk: At 2 years, the rates of discontinuation were balanced, but permanent discontinuation was12% lower in the apixaban group than in the aspirin group.
Are reports of the study free of suggestion of selective outcome reporting? All pre-specified outcomes reported?	Low risk: All outcomes appear to have been reported.	Not reported	Low risk: All outcomes appear to have been reported	Not reported	Low risk: All outcomes appear to have been reported
Was the study apparently free of other problems that could put it at a high risk of bias?[60]	The subgroup analysis was pre-specified. Only one other subgroup analysis appears to have been conducted (duration). The subgroup analysis included almost all patients who were randomised.	The subgroup analysis was a *post hoc* analysis and the focus of this publication. It is not clear if other subgroup analyses were conducted.	It was not reported if the subgroup of interest was pre-specified or conducted *post hoc*.	The subgroup analysis was a *post hoc* analysis and the focus of this publication. It is not clear if other subgroup analyses were conducted.	This paper appears to be an exploratory analyses using data from two studies.

[60] As these publications focused on subgroup analyses, we addressed any potential problems with these types of analyses within this criterion.

Overall risk of bias assessment	Low, but results obtained from subgroup analyses should be considered exploratory.	Low, but results obtained from subgroup analyses should be considered exploratory.	Unclear, but results obtained from subgroup analyses should be considered exploratory.	Low, but results obtained from subgroup analyses should be considered exploratory.	Low, but results obtained from subgroup analyses should be considered exploratory.

Table 3.17: Question 1a: Detailed risk of bias table for case-control studies (CRD)

	Studies
	Baturova 2014 [12]
Is the case definition explicit?	Low risk: Cases were defined as first ever ischaemic stroke patients.
Has the disease state of the cases been reliably assessed and validated?	Low risk: Patients with all first-ever-in-life strokes were diagnosed in accordance with WHO definition and confirmed by CT/ MR/autopsy examination of the brain. Information about AF before or at admission for acute ischemic stroke (stroke group) or enrolment in the register (control group) was obtained from electronic medical records, ECG recordings retrieved from the regional electronic ECG database and by record linkage with the Swedish Hospital Discharge Register.
Were the controls randomly selected from the source of population of the cases?	Low risk: Control subjects were randomly selected from the same geographical region and matched to Lund Stroke Register cases for the year 2001 by age and gender in a 1:1 case-control manner using the Swedish Population Register.
How comparable are the cases and controls with respect to potential confounding factors?	Low risk: Stroke patients had higher rates of risk factors compared to controls which is what would be expected.
Were interventions and other exposures assessed in the same way for cases and controls?	NA
How was the response rate defined?	NA
Were the non-response rates and reasons for non-response the same in both groups?	NA
Is it possible that over-matching has occurred in that cases and controls were matched on factors related to exposure?	Low risk: Controls were matched using age and gender.

Was an appropriate statistical analysis used (matched or unmatched)?	Low risk: To identify clinical predictors of ischemic stroke, significantly associated covariates were evaluated in univariate logistic regression models with estimation of odds ratios and likelihood-ratio tests. To determine independent predictors of ischaemic stroke, clinical factors significantly associated with stroke in the univariate models were subsequently included in a stepwise regression analysis with backwards elimination.

AF: Atrial fibrillation; ECG: electrocardiogram; CT: Computerised tomography; MR: Magnetic resonance; NA: Not applicable

Table 3.18: Question 1a: Detailed risk of bias table for cohort studies (CASP Cohort Study Checklist)

	Studies		
	Banerjee 2013 [11]	**Lip 2014 [16]; Proietti 2017 [18]**	**Meinertz 2011 [17]**
1. Did the study address a clearly focused issue?	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.
2. Was the cohort recruited in an acceptable way?	Yes: All patients diagnosed with non-valvular atrial fibrillation or atrial flutter in a department of cardiology over a specified time period.	Yes: The registry population comprised consecutive in- and out-patients with AF presenting to cardiologists in participating ESC countries.	Yes: Data from patients with AF seen by 730 physicians representing a random sample of all primary care physicians in Germany.
3. Was the exposure accurately measured to minimise bias?	NA	NA	NA
4. Was the outcome accurately measured to minimise bias?	Yes: The authors stated that $CHADS_2$ and CHA_2DS_2-VAS_C scores were calculated. Details are provided. They also stated that information on study outcomes 'was recorded', but no further details were reported.	Yes: Outcome was objective, but no details on methods used to diagnose stroke were reported.	Yes?: The authors stated that the $CHADS_2$ and CHA_2DS_2-VAS_C scores were computed using available information.
5. (a) Have the authors identified all important confounding factors?	Yes, but the authors stated that their study did not include "changes in pattern of NVAF over time during the study period."	Yes	NA
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes: The authors conducted regression analyses.	Yes: The authors conducted regression analyses.	NA

6. (a) Was the follow up of subjects complete enough?	NA	Of 3119 patients from 9 countries, 467 were lost to follow-up at one year; "although full data on clinical subtype of AF was available for 3049 patients" Clinical status during the second-year follow-up was available for 1990 (64.0%) patients. Of these, 101 (5.1%) died and 1889 had at least one visit/contact during the second-year follow-up. *Figures reported not entirely clear*	NA
6. (b) Was the follow up of subjects long enough?	NA	Yes: up to 2 years follow-up.	NA
7. What are the results of this study?	The authors stated that compared with paroxysmal NVAF, rates of stroke/TE, bleeding and all-cause mortality (p<0.001) were significantly higher in permanent NVAF patients but not in persistent NVAF patients.	The authors stated that after 1 year, 5.7% (177/3119) of the patients enrolled in the study died between the time of enrolment and the 1-year follow-up visit. The highest mortality rates were in the first detected (7.5%) and in the long-standing persistent AF (8.3%) groups. (These data do not clearly match with information presented in a table).	Only baseline data presented
8. How precise are the results?	Confidence intervals are relatively narrow.	Not clear	NA
9. Do you believe the results?	Appear to be reliable.	It is very hard to interpret the data because the denominators presented vary.	NA
10. Can the results be applied to the local population?	Yes	Yes	NA
11. Do the results of this study fit with other available evidence?	The authors stated that "rates of stroke, TE and death differed significantly by patterns of NVAF. However, only previous stroke,	In terms of patterns of stroke risk, the results are consistent with the other studies. Data on mortality rates are not directly comparable	Only data for stroke risk were presented in this study. These results are comparable to the other available evidence

	age, heart failure and vascular disease (not pattern of NVAF) independently increased risk of adverse outcomes in multivariate analyses. Thus, stroke risk is similar across all patterns of NVAF and antithrombotic therapy should be based on clinical risk factors, not on arrhythmia pattern." The first sentence fits with the other available evidence, but similar multivariable analysis was not done across all the other studies, so difficult to compare against the authors final comment.	as not expressed as a rate per 100 patient years.	
12. What are the implications of this study for practice?	The authors stated that antithrombotic therapy should be based on clinical risk factors, not on arrhythmia pattern.	The authors stated that compliance with the treatment guidelines for patients with the lowest (CHA2DS2-VASc=0) and higher stroke risk scores remained suboptimal.	The authors stated that patients with AF managed in primary care often receive guideline-conforming therapy including antithrombotic therapy, rate control and rhythm control. Despite this apparent adherence, almost half of the patients were hospitalized in the year prior to enrolment, suggesting that the therapies applied do not stabilise patients sufficiently to keep them out of hospital.

AF: Atrial fibrillation; NVAF: Non-valvular atrial fibrillation; TE: Thromboembolism

Table 3.19: Question 1b: Detailed risk of bias for RCTs (Cochrane) *with relevant subgroup analysis*

	Study
	Rienstra 2014 [22]
Was the allocation sequence adequately generated?	Unclear risk: Described as randomised but method of randomisation is not reported.
Was allocation adequately concealed?	Unclear risk: Allocation concealment was not reported.
Were the care providers and/or participants blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	Unclear risk: Blinding was not reported.
Were the outcome assessors blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	Low risk: A committee of experts who were unaware of the treatment assignments, adjudicated all reported end points.
Incomplete outcome data - Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	Low risk: Withdrawals were balanced across groups; eight patients in the rate-control group and nine in the rhythm-control group withdrew from the study early
Are reports of the study free of suggestion of selective outcome reporting? All pre-specified outcomes reported?	Low risk: All pre-specified outcomes appear to have been reported.
Was the study apparently free of other problems that could put it at a high risk of bias?[61]	The subgroup analysis was *post-hoc*. No other subgroup analysis appears to have been conducted, but several outcomes were assessed.
Overall risk of bias assessment	Unclear risk of bias, but results obtained from subgroup analyses should be considered exploratory

NR: not reported

[61] We addressed any potential problems with subgroup analyses within this criterion

Table 3.20: Question 1b: Detailed risk of bias table for cohort studies (CASP Cohort Study Checklist)

	Study
	Potpara 2013[21]
1. Did the study address a clearly focused issue?	Yes: Question clearly focused in terms of population and outcomes
2. Was the cohort recruited in an acceptable way?	Yes: Single-centre registry-based study of consecutive first-diagnosed AF patients.
3. Was the exposure accurately measured to minimise bias?	NA
4. Was the outcome accurately measured to minimise bias?	Yes: Detailed diagnostic evaluation was performed at baseline and at regular annual follow-up visits.
5. (a) Have the authors identified all important confounding factors?	Yes
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	Yes: The authors conducted regression analyses.
6. (a) Was the follow up of subjects complete enough?	All patients completed a 5-year follow-up, and 251 (22.8%) were lost for further follow-up beyond 5 years.
6. (b) Was the follow up of subjects long enough?	Yes: 10 years
7. What are the results of this study?	The authors stated that "Kaplan–Meier 10-year estimates of ischaemic stroke (log-rank test = 6.2, p = 0.013) were significantly worse for patients with asymptomatic AF compared to those with symptomatic arrhythmia. In the multivariable Cox regression analysis, intermittent asymptomatic AF was significantly associated with progression to permanent AF (Hazard Ratio 1.6; 95% CI, 1.1–2.2; p = 0.009)."
8. How precise are the results?	Confidence intervals are relatively narrow.
9. Do you believe the results?	Appear to be reliable.
10. Can the results be applied to the local population?	Yes
11. Do the results of this study fit with other available evidence?	No other study reported on stroke; results for stroke risk are inconsistent with Rienstra (2014), and data on death from cardiovascular causes is consistent with this other study.
12. What are the implications of this study for practice?	The authors stated that in a 'real-world' setting, patients with asymptomatic presentation of their first-diagnosed AF could have different risk profile and long-term outcomes compared to those with symptomatic AF.

AF: Atrial fibrillation; CI: Confidence interval; NA: Not applicable

Question 2

No studies met the inclusion criteria for this question.

Question 3

Table 3.21: Question 3: Detailed risk of bias for SRs (AMSTAR 2)

AMSTAR criterion	Response
	Welton 2017 [26]
Did the research questions and inclusion criteria for the review include the components of PICO?	Yes
Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did the report justify any significant deviations from the protocol?	Yes - The protocol for the systematic review was registered with the NIHR international prospective register of scientific reviews (PROSPERO) registration no. CRD42014013739
Did the review authors explain their selection of the study designs for inclusion in the review?	Yes – The authors included cross sectional, case-control, cohort studies and RCTs recruiting at least 40 adults who had not sought medical attention on account of symptoms associated with AF (with the exception of cases in case–control studies).
Did the review authors use a comprehensive literature search strategy?	Yes - MEDLINE and PreMEDLINE, EMBASE, The Cochrane Library's CENTRAL and CINAHL. Reference and citation tracking were undertaken to identify further relevant studies. When necessary, the SR authors stated that they contacted lead authors for more information on published and unpublished studies that might be relevant.
Did the review authors perform study selection in duplicate?	Yes - Articles were screened independently by two reviewers. In all cases, disagreements were discussed between the two reviewers and, if not resolved, resolution was sought through the involvement of a third reviewer. Full texts of the studies included at the screening stage were also selected independently by two reviewers
Did the review authors perform data extraction in duplicate?	Partially - Data extraction was conducted by one reviewer and then reviewed by a second reviewer. Disagreements were discussed

	between the two reviewers and, if not resolved, resolution was sought through the involvement of a third reviewer.
Did the review authors provide a list of excluded studies and justify the exclusions?	Yes - the excluded studies are summarised in an appendix
Did the review authors describe the included studies in adequate detail?	Yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes - Risk of bias was assessed using the QUADAS-2 tool
Did the review authors report on the sources of funding for the studies included in the review?	Not reported
If meta-analysis was justified did the review authors use appropriate methods for statistical combination of results?	Yes – methods for meta-analysis are reported in the main body of the text and in detail in an appendix.
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Not reported
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	The review was funded by the NHS and individual review authors provided details about their personal conflicts of interest including funding for any funding received,

Table 3.22: Question 3: Detailed risk of bias table for diagnostic accuracy studies (QUADAS-2)

Reference	Was the spectrum of patients representative of the patients who will receive the test in practice?	Is the reference standard likely to classify the target condition correctly?	Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	Did the whole sample or a random selection of the sample, receive verification using the intended reference standard?	Did patients receive the same reference standard irrespective of the index test result?	Were the reference standard results interpreted without knowledge of the results of the index test?	Were the index test results interpreted without knowledge of the results of the reference standard?.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	Were uninterpretable/ intermediate test results reported?	Were withdrawals from the study explained?
Hald 2017 [23]	Low: Participants were people attending their own GP practice. Likely representative of opportunistic screening.	Low: 12-lead ECG is the gold standard	Unclear: Not reported. Assume 12-lea ECG was conducted the same day	High: Only those who had an irregular pule went on to have an ECG	Low: Patients who had an irregular pulse all had 12-lead ECG	Low: The ECG recordings were collected post study for blinded specialist examination performed by two skilled AF specialists	Low: The index test was conducted before the reference standard	Low: Conducted among participants in their own GP practice.	Unclear: There didn't appear to be any uninterpretable results	N/A: No withdrawals

Kristensen 2016 [24]	Low: Participants were people attending their own GP practice. Likely representative of opportunistic screening.	Low: 12-lead ECG is the gold standard	Low: Index test and reference standard conducted simultaneously	Low: All patients had the index test and reference standard	Low: All patients received the same reference standard	Low: The trainee GPs who analysed the PEM recordings were blinded to the results of the 12-lead ECG	Low: The 12-lead ECG read by a cardiologist and a senior GP were blinded to the PEM results	Low: Conducted in the participants GP practice. After finishing the blinded analysis the investigators obtained information from patient medical records on relevant rhythm-controlling medication and diagnosis to determine study population demographics.	Low: Four patients were excluded due to poor ECG quality. A further three patients were re-evaluated when there was found to be no match between the ECG and the PEM	NA: No withdrawals
Svennberg 2017 [25]	Low: All people in one geographic revgion born in	High: The reference standard was interpretation of an	Unclear: Time period not reported	Low: Only those who had irregular rhythm or minor	Low: Patients who had an irregular pulse all	Low: The cardiologists were blinded to the results of	Low: The index test was a compute	Unclear: Participants took their own measurem	Low: Uninterpretable results were reported and investigated	Low: Some participants withdrew consent.

	1936 or 1937 were invited to participate	ECG from a hand-held device	rhythm deviations according to the algorithm, or manually interpreted by a specialist nurse received interpretation by a cardiologist (reference standard). Interpretation skill of the nurses were randomly checked.	had cardiologist interpretation of their ECG	the algorithm	r-based algorithm	ents at home

ECG - electrocardiogram

Question 4

Table 3.23: Question 4: Detailed risk of bias for SRs (AMSTAR 2)

	Studies		
	Moran 2013[29]; 2016 [9] (Cochrane)	**Moran 2015 [30] (HTA)** (methodology of Cochrane and HTA were the same, but results presented in HTA were brief and details of additional two studies in the HTA not fully reported)	**Welton 2017 [26] (HTA)**
Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	Yes	Yes
Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did the report justify any significant deviations from the protocol?	Yes – A protocol was published	Yes	Yes - The protocol for the systematic review was registered with the NIHR international prospective register of scientific reviews (PROSPERO) registration no. CRD42014013739
Did the review authors explain their selection of the study designs for inclusion in the review?	Yes	Yes	Yes – The authors originally planned to include all of the study designs that were considered by the original Cochrane review (RCTs, cluster RCTs, controlled before-and-after studies and interrupted time series). However, the Cochrane update was restricted to RCTs only (Patrick Moran, personal communication). The authors changed their inclusion criteria to focus solely on RCTs.
Did the review authors use a comprehensive literature search strategy?	Yes – CENTRAL, MEDLINE and MEDLINE In-Process, EMBASE CINAHL, EBSCO,	Yes – CENTRAL, MEDLINE and MEDLINE In-Process, EMBASE CINAHL, EBSCO, trial registries	Yes - MEDLINE and PreMEDLINE, EMBASE, The Cochrane Library's CENTRAL and

	trial registries and conference abstract were searched. In addition, the authors searched the reference lists of all included papers to identify potentially relevant articles. When required, the authors contacted lead authors and investigators to ask for information about additional published or unpublished studies that may be relevant.	and conference abstract were searched. In addition, the authors searched the reference lists of all included papers to identify potentially relevant articles. When required, the authors contacted lead authors and investigators to ask for information about additional published or unpublished studies that may be relevant.	CINAHL. Reference and citation tracking were undertaken to identify further relevant studies. They SR authors stated that when necessary, they contacted lead authors for more information on published and unpublished studies that might be relevant.
Did the review authors perform study selection in duplicate?	Yes – Two review authors independently assessed the eligibility of studies and identified multiple reports from single studies, resolving disagreements by discussion.	Yes – Two review authors independently assessed the eligibility of studies and identified multiple reports from single studies, resolving disagreements by discussion.	Yes – Articles were screened in parallel by two reviewers. In all cases, disagreements were discussed between the two reviewers and, if not resolved, resolution was sought through the involvement of a third reviewer.
Did the review authors perform data extraction in duplicate?	Yes – Two review authors independently extracted data, resolving disagreements by discussion.	Yes – Two review authors independently extracted data, resolving disagreements by discussion.	Partially – Data extraction was conducted by one reviewer and then reviewed by a second reviewer. Disagreements were discussed between the two reviewers and, if not resolved, resolution was sought through the involvement of a third reviewer.
Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	No	Not for individual studies (overall numbers and reasons were reported)
Did the review authors describe the included studies in adequate detail?	Yes	No	Yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB)	Yes – Risk of bias was assessed using the Cochrane tool	Yes – Risk of bias was assessed using the Cochrane tool	Yes – Risk of bias was assessed using the Cochrane tool

in individual studies that were included in the review?			
Did the review authors report on the sources of funding for the studies included in the review?	Yes	No	Not reported
If meta-analysis was justified did the review authors use appropriate methods for statistical combination of results?	NA	NA	NA (for outcomes relevant to this NSC review)
If meta-analysis was performed did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	NA	NA	NA (for outcomes relevant to this NSC review)
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes	Yes	Yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	NA – only one study included in the review	Yes – The authors stated that the studies used different screening tests in different populations, so the results could not be combined	Data were not combined; each study was reported separately
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	NA	NA	NA
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	The authors reported that there were no conflicts of interest. Funding was not reported.	The authors reported that there were no conflicts of interest. Funding was not reported.	The review was funded by the NHS and individual review authors provided details about their personal conflicts of interest

	including funding for any funding received,

NA: Not applicable; RCT: Randomised controlled trial

Table 3.24: Question 4: Detailed risk of bias for RCTs (Cochrane)

	Studies	
	González Blanco 2017 [27]	**Halcox 2017 [28]**
Was the allocation sequence adequately generated?	Randomization was centralized and stratified by type of healthcare professional (physician versus nurse) using the EPIDAT 3.1 software package.	Yes – central randomisation (likely computer generated)
Was allocation adequately concealed?	Yes – The authors stated that consecutive sampling was performed by professionals for patient selection.	Yes – randomisation was undertaken via an Interactive Voice Recognition Service.
Were the care providers and/or participants blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	No - Patients included in the study were informed of the goal of the study	Participants knew if that had received the intervention – but outcomes were objective, so lack of blinding may not necessarily affected results.
Were the outcome assessors blind to treatment allocation? If not, what might be the likely impact on the risk of bias?	Not reported, but unlikely as patients not blinded	Not reported
Incomplete outcome data - Were there any unexpected imbalances in drop-outs between groups? If so, were they explained or adjusted for?	Not reported – it appears that all patients were included	Very few withdrawals/drop-outs were reported: 3 participants in the iECG arm withdrew (1 after completing the 12-week and 2 after the 12- and 32-week follow-up calls), and 2 were lost to follow-up (1 after participation in the 12-week and 1 after the 12- and 32-week follow-up). All other patients completing the study participated fully in all telephone interviews at 12, 32, and 52 weeks except for 1 follow-up call missed at 32 weeks by an iECG participant.
Are reports of the study free of suggestion of selective outcome reporting? All pre-	Not clear – only one primary outcome reported in the methods section, although some additional results are presented. It is not clear if the authors also specifically aimed to assess this outcome.	All outcomes described in the methods section were included in the analysis, but hazard ratios were not presented for all comparisons.

specified outcomes reported?		
Was the study apparently free of other problems that could put it at a high risk of bias?	No – Patients' mean age was higher in the control group compared to the experimental group (75.61 vs 74.07; p < 0.001). The authors stated that a difference was observed in the comparison of groups by age, as there were more patients in the 80–85 year and >85 years category in the control group (9.3% vs 5.6%). A higher number of cardiovascular risk factors and associated morbidity (obesity, alcoholism, tobacco use, heart failure, hyperthyroidism and valvular heart disease) were observed in control group patients, as compared to experimental group patients. No - The sample size in the study was below the size needed (n=12,870 patients), although the authors believe that the study had enough statistical power to test their statistical hypothesis.	Yes - The authors reported that age, sex, and clinical characteristics were similar between the two groups. A sample size of 500 participants per study arm was estimated to provide 92% power to detect a significant difference (α=5%) in the time to AF diagnosis between groups – this sample size was met. The study was funded in part by a project grant from AliveCor, but data were analysed and reported independently. No - The authors noted, however, closer contact between the study team and the iECG participants – and that this closer contact would make it more likely that relevant events may have been missed in the routine care patients.
Overall risk of bias assessment	High	Low

AF: Atrial fibrillation; iECG: ipod electrocardiogram

Question 5

Table 3.25: Question 5: Detailed risk of bias for cost-effectiveness studies (adapted from Drummond 1996)

Risk of bias criterion		
Welton 2017 [26]		
1. Was the research question stated?	Yes	What is the cost-effectiveness of AF screening?
2. Was the economic importance of the research question stated?	Yes	The economic impact of AF screened had to be defined
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Yes	NHS
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	A range of screening stategies was considered

5. Were the alternatives being compared clearly described?	Yes	Screening procedures described
6. Was the form of economic evaluation stated?	Yes	Cost-utility analysis
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	Yes	Impact on quality of life of consequences of AF
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	Sources of data were reported for all inputs of the model
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	Partly	Some studies were fully described, other studies only mentioned
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	NA	Extensive details on the systematic review were reported
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Yes	QALYs
12. Were the methods used to value health states and other benefits stated?	Yes	Details were provided
13. Were the details of the subjects from whom valuations were obtained given?	Yes	Characteristics of patients with detected AF were provided
14. Were productivity changes (if included) reported separately?	No	Productivity losses were not considered
15. Was the relevance of productivity changes to the study question discussed?	No	See previous comment
16. Were quantities of resources reported separately from their unit cost?	Yes	Extensive information on unit costs and quantities of resources used was given
17. Were the methods for the estimation of quantities and unit costs described?	Yes	Sources described and some methods to derive costs were also reported
18. Were currency and price data recorded?	Yes	Year 20145, UK pounds sterling
19. Were details of price adjustments for inflation or currency conversion given?	Yes	The price year was 2014
20. Were details of any model used given?	Yes	The authors described the decision model
21. Was there a justification for the choice of model used and the key parameters on which it was based?	Yes	The authors explained the appropriateness of the model
22. Was the time horizon of cost and benefits stated?	Yes	Lifetime
23. Was the discount rate stated?	Yes	3.5% for both costs and benefit
24. Was the choice of rate justified?	No	No justification was provided
25. Was an explanation given if cost or benefits were not discounted?	NA	Discounted
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	No	Not provided

27. Was the approach to sensitivity analysis described?	Yes	Deterministic analyses were conducted
28. Was the choice of variables for sensitivity analysis justified?	Yes	Key parameters were varied
29. Were the ranges over which the parameters were varied stated?	Yes	Provided
30. Were relevant alternatives compared? (That is, were appropriate comparisons made when conducting the incremental analysis?)	Yes	Various screening strategies vs no screening
31. Was an incremental analysis reported?	Yes	ICER
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Partly	Incremental results were reported
33. Was the answer to the study question given?	Yes	The ICERs of all screening strategies were reported
34. Did conclusions follow from the data reported?	Yes	Confirmed by the robustness of results
35. Were conclusions accompanied by the appropriate caveats?	Yes	Limitations extensively acknowledged by the authors
36. Were generalisability issues addressed?	Partly	The authors compared their results with those of other studies

Question 6

Table 3.26: Question 6a: Detailed risk of bias table for cohort studies (CASP Cohort Study Checklist)

Criterion	Studies				
	Das 2015 [31]	**Hodgkinson 2011** [32]	**Johnson 2016** [33]	**Martinez 2016** [34]	**Mueller 2017** [35]
1. Did the study address a clearly focused issue?	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes,	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.
2. Was the cohort recruited in an acceptable way?	Yes: Cohort of patients from 65 general practices.	Yes: Data from the General Practice Research Database was analysed.	Yes: Data from the General Practice Research Datalink was analysed.	Yes: Data from the General Practice Research Datalink was analysed.	Yes: The study used linked data from PIS and SMR01.
3. Was the exposure accurately measured to minimise bias?	Yes	NA	NA	NA	NA

4. Was the outcome accurately measured to minimise bias?	Yes	Yes	Yes: Definition of OAC treatment persistence was provided (although the authors note that assumptions have to be made).	Yes: Definition of OAC treatment persistence was provided.	Yes: Definitions and calculation methods were provided for the main outcomes of discontinuation, persistence and adherence.
5. (a) Have the authors identified all important confounding factors?	No	No	Yes (although the authors stated that there are limitations to using primary data such as missing data which can contribute to residual confounding).	Yes	Yes
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	NA	NA	NA	NA	NA
6. (a) Was the follow up of subjects complete enough?	No: Only 8 of 65 practices were included in the analysis.	NA (retrospective analysis)	NA (retrospective analysis)	NA (retrospective analysis)	NA (retrospective analysis)
6. (b) Was the follow up of subjects long enough?	Yes: The authors aimed to evaluate the service over 2 years.	Yes: Data over 1 and 5 years was evaluated.	Yes:12 months	Yes: Mean follow-up was 1.9 ± 1.1 years.	Yes: median follow-up time was 228 days (IQR 105-425).
7. What are the results of this study?	The authors stated "audit of eight practices after 195 (185–606) days showed that 90% of patients started on a new anticoagulant	The authors stated that they found "no relationship between maintenance or discontinuation of anticoagulants and stroke risk as	At the end of follow-up, persistence ranged from 62.5% to 82.8% across different treatments.	The authors stated that "Persistence with OAC declined over 12 months to 63.6 % for VKA and 79.2 % for NOAC (p< 0.0001). Persistence for those	The authors stated that "adherence to DOAC treatment was good, and switching from DOAC to warfarin was low. However,

	therapy had continued treatment."	measured using $CHADS_2$ scores in this cohort of patients with AF."		with $CHA2DS_2VASc \geq 2$ was significantly greater for NOAC (83.0 %) than VKA (65.3 %, $p< 0.0001$) at one year and all earlier time points."	discontinuation and persistence rates were variable."
8. How precise are the results?	NA	NA	Percentages with relatively narrow confidence intervals were reported.	NA	NA
9. Do you believe the results?	Unclear as only 8 of 65 practices were included in the analysis	Yes	Yes	Yes	The results appear to be reliable within the specified patient group (see below).
10. Can the results be applied to the local population?	Yes	Yes	Yes (OAC naïve patients)	Yes	No: The patients included in the study in were only in secondary care.
11. Do the results of this study fit with other available evidence?	The authors reported that 1.5% declined treatment and that there was 90% compliance in patients who were not previously taking anticoagulation but were eligible to do so.	The authors stated that "the lack of relationship between treatment pathways involving anticoagulant use and $CHADS_2$ scores reiterates the findings of much previous research regarding the underuse of warfarin."	These results are similar to Martinez 2016 and Mueller 2017(the other studies that reported on persistence).	Yes	The authors stated that there were two differences: "First, adherence to treatment was considerably higher in our study than has been reported in other studies conducted on a national level; and second, switches from DOACs to VKAs were much less common than in previous observational studies."

12. What are the implications of this study for practice?	The authors stated that "systematic identification of patients with AF with high stroke-risk and consultation in PCAF consultant-led clinics effectively delivers oral anticoagulation to high-risk patients with AF in the community."	The authors stated "the results of this study provides further grist to the argument that more education is needed about the most appropriate management of AF."	No implications for practice were reported.	The authors stated that "persistence was significantly higher with NOAC than VKA, and could alone lead to fewer cardioembolic strokes."	No implications for practice were reported.

AF: Atrial fibrillation; DOAC: Direct oral anticoagulant; VKA: Vitamin K antagonists; NA: Not applicable; PCAF: Primary care AF (service)

Table 3.27: Question 6b: Detailed risk of bias table for cohort studies (CASP Cohort Study Checklist)

Criterion	**Studies**					
	Das 2015 [31]	**Induruwa 2017** [37]	**Isaew 2017** [38]	**Lonsdale 2016** [41]	**Martinez 2016** [34]	**Mazurek 2017** [42]
1. Did the study address a clearly focused issue?	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.	Yes: Question clearly focused in terms of population and outcomes.
2. Was the cohort recruited in an acceptable way?	Yes: Cohort of patients from 65 general practices.	Yes: Data from screening study within a hospital	Yes: Data from The Health Improvement Network (THIN).	Yes: Data from the General Practice Research Datalink was analysed.	Yes: Data from the General Practice Research Datalink was analysed.	Yes: Cohort of patients from 11 general practices.
3. Was the exposure accurately measured to minimise bias?	Yes	NA	NA	Yes	NA	NA
4. Was the outcome accurately measured to minimise bias?	Yes	Yes	Yes	Yes	Yes: Definition of OAC treatment persistence was provided.	Yes

5. (a) Have the authors identified all important confounding factors?	No	NA	Yes	No	Yes	No
5. (b) Have they taken account of the confounding factors in the design and/or analysis?	No	NA	NA	No	NA	NA
6. (a) Was the follow up of subjects complete enough?	Yes	NA (only baseline data extracted)	NA (retrospective analysis)	Yes	NA (retrospective analysis)	NA (only baseline data extracted)
6. (b) Was the follow up of subjects long enough?	Yes: The authors aimed to evaluate the service over 2 years.	NA	Yes: Data was collected for a 15 year time period.	Yes: Data were collected for just over a year.	Yes: Mean follow-up was 1.9 ± 1.1 years.	NA
7. What are the results of this study?	The authors stated "the overall proportion of eligible patients receiving anticoagulation improved from 77% to 95%."	NA (main results presented by the study authors are not of interest to this NSC review)	The authors stated: "Among patients with a CHADS2 score of ≥1, between 2000 and 2015 the proportion prescribed anticoagulants increased from 18.8% (95% CI 16.4 to 21.4) to 56.2% (95% CI 55.0 to 57.3) and from 34.2% (95% CI 33.3 to 35.0) to 69.4% (95% CI 68.9 to 69.8) in patients	The authors stated that " the CCG has an average of 71.4% of high risk patients on an anticoagulant, variation between practices has been reduced and 14 practices have prescribing rates above 70%."	The authors stated that "OAC prescriptions for $CHA2DS_2VASc$ score ≥ 2 (guideline adherence) increased from 41.2 % to 65.5 %."	NA (main results presented by the study authors are not of interest to this NSC review)

			with paroxysmal and other (persistent/ permanent) AF, respectively."			
8. How precise are the results?	NA	NA	Percentages with relatively narrow confidence intervals were reported.	NA	NA	NA (for outcome of interest to this NSC review)
9. Do you believe the results?	Yes	Yes	Yes	No (it is not clear how data were calculated for 2014 and information in text and tables to not tally)	Yes	Yes
10. Can the results be applied to the local population?	Yes	Yes	Yes	No (data specific to Fylde and Wyre)	Yes	Yes, but may not be representative of other regions.
11. Do the results of this study fit with other available evidence?	The authors reported high rates of prescribing for patient with AF.	The authors reported that 56% AF patients were on anticoagulation treatment.	Yes (agreement with other studies is discussed by the authors)	Yes	Yes	The authors reported that "approximately half of eligible patients with AF are prescribed oral anticoagulation in line with guidelines."
12. What are the implications of this study for practice?	The authors stated that "based on extrapolated data from	The authors stated that "secondary care screening for AF targets a high	Not stated, but the authors note "The question remains	No explicitly stated, but the authors stated "The change seen in the	The authors stated in their conclusions that persistence with therapy may be	The authors stated "Guideline-adherent antithrombotic

	previous studies, around 30-35 strokes per year may have been prevented in these previously under-treated high-risk patients.”	risk population, is accurate and cost-effective, and enables us to critically look at barriers to anticoagulation, as well as allowing a more efficient and collaborative approach to support primary care colleagues in reducing risk of cardioembolic strokes.”	as to whether the difference in treatment between patients with paroxysmal AF and patients with other AF is the result of lower levels of treatment initiation by clinicians or whether patients with paroxysmal AF are more likely to stop their treatment, and to explore the reasons why.”	prescribing rates of anticoagulants in AF across all patient risk groups demonstrates that NICE CG180 has successfully been implemented in the CCG with regards to prescribing anticoagulants for stroke prevention.”	as crucial a factor in efforts to reduce stroke in AF, as increasing the overall proportion of prescribed OACs.	treatment significantly reduces the risk of stroke among primary prevention patients and both risk of recurrent stroke and death in patients with previous stroke.”

AF: Atrial fibrillation; CCG: Clinical Commissioning Group: NA: Not applicable; OAC: Oral anticoagulant

Appendix 4 – UK NSC reporting checklist for evidence summaries

All items on the UK NSC Reporting Checklist for Evidence Summaries have been addressed in this report. A summary of the checklist, along with the page or pages where each item can be found in this report, is presented in Table 4.

Table 4. UK NSC reporting checklist for evidence summaries

	Section	Item	Page no.
1.	TITLE AND SUMMARIES		
1.1	Title sheet	Identify the review as a UK NSC evidence summary.	Title page
1.2	Plain English summary	Plain English description of the executive summary.	5
1.3	Executive summary	Structured overview of the whole report. To include: the purpose/aim of the review; background; previous recommendations; findings and gaps in the evidence; recommendations on the screening that can or cannot be made on the basis of the review.	6
2.	INTRODUCTION AND APPROACH		
2.1	Background and objectives	Background – Current policy context and rationale for the current review – for example, reference to details of previous reviews, basis for current recommendation, recommendations made, gaps identified, drivers for new reviews Objectives – What are the questions the current evidence summary intends to answer? – statement of the key questions for the current evidence summary,	13

		criteria they address, and number of studies included per question, description of the overall results of the literature search. Method – briefly outline the rapid review methods used.	
2.2	Eligibility for inclusion in the review	State all criteria for inclusion and exclusion of studies to the review clearly (PICO, dates, language, study type, publication type, publication status etc.) To be decided *a priori*.	17
2.3	Appraisal for quality/risk of bias tool	Details of tool/checklist used to assess quality, e.g. QUADAS 2, CASP, SIGN, AMSTAR.	24
3.	SEARCH STRATEGY AND STUDY SELECTION (FOR EACH KEY QUESTION)		
3.1	Databases/ sources searched	Give details of all databases searched (including platform/interface and coverage dates) and date of final search.	24 and Appendix 1
3.2	Search strategy and results	Present the full search strategy for at least one database (usually a version of Medline), including limits and search filters if used. Provide details of the total number of (results from each database searched), number of duplicates removed, and the final number of unique records to consider for inclusion.	Appendix 1 26
3.3	Study selection	State the process for selecting studies – inclusion and exclusion criteria, number of studies screened by title/abstract and full text, number of reviewers, any cross checking carried out.	Question 1: 28 Question 2: 50 Question 3: 53 Question 4: 63 Question 5: 69 Question 6: 77

4.	STUDY LEVEL REPORTING OF RESULTS (FOR EACH KEY QUESTION)		
4.1	Study level reporting, results and risk of bias assessment	For each study, produce a table that includes the full citation and a summary of the data relevant to the question (for example, study size, PICO, follow-up period, outcomes reported, statistical analyses etc.). Provide a simple summary of key measures, effect estimates and confidence intervals for each study where available. For each study, present the results of any assessment of quality/risk of bias.	Study level reporting: Appendix 3 Quality assessment: Appendix 3
4.2	Additional analyses	Describe additional analyses (for example, sensitivity, specificity, PPV, etc.) carried out by the reviewer.	N/A
5.	QUESTION LEVEL SYNTHESIS		
5.1	Description of the evidence	For each question, give numbers of studies screened, assessed for eligibility, and included in the review, with summary reasons for exclusion.	Question 1: 30 – 48 Question 2: 50 - 52 Question 3: 53 - 62 Question 4: 63 - 68 Question 5: 69 - 76 Question 6: 77 - 81
5.2	Combining and presenting the findings	Provide a balanced discussion of the body of evidence which avoids over reliance on one study or set of studies. Consideration of four components should inform the reviewer's judgement on whether the criterion is 'met', 'not met' or 'uncertain': quantity; quality; applicability and consistency.	Question 1: 30 – 48 Question 2: 50 - 52 Question 3: 53 - 62 Question 4: 63 - 68 Question 5: 69 - 76

			Question 6: 77 – 81
5.3	Summary of findings	Provide a description of the evidence reviewed and included for each question, with reference to their eligibility for inclusion. Summarise the main findings including the quality/risk of bias issues for each question. Have the criteria addressed been 'met', 'not met' or 'uncertain'?	Question 1: 49 Question 2: 52 Question 3: 62 Question 4: 68 Question 5: 76 Question 6: 82
6.	REVIEW SUMMARY		
6.1	Conclusions and implications for policy	Do findings indicate whether screening should be recommended? Is further work warranted? Are there gaps in the evidence highlighted by the review?	87 - 88
6.2	Limitations	Discuss limitations of the available evidence and of the review methodology if relevant.	88 - 89

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