UNIVERSITY OF NOTTINGHAM

SCHOOL OF MEDICINE

PHD: PRIMARY CARE

SCREENING FOR ATRIAL

FIBRILLATION IN PRIMARY CARE

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Declarations

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Contents

Tables

Figures

Appendices

List of abbreviations

AF	Atrial fibrillation
ANOVA	Analysis of variance
AUD	Australian dollar
BPM	Blood Pressure monitor
C	Cohort
CC	Case-control
CCG	Clinical Commissioning Group
CI	Confidence interval
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CS	Cross-sectional
DOACS	Direct oral anticoagulants
ECG	Electrocardiogram
EHRA	European Heart Rhythm Association
EORP-AF	EurObservational Research Programme - Atrial Fibrillation
EQ-5D	EuroQol five dimensions
ES	European Society of Cardiology
GP	General practitioner
HCA	Healthcare assistant
HCP	Healthcare professional
HPV	Human Papilloma Virus

HR	Hazard ratio
ICER	Incremental Cost-Effectiveness Ratio
IQR	Interquartile range
KSA	Knowledge, skills and attitudes
MACE	Major Adverse Cardiac Events
MRC	Medical Research Council
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NLR	Negative Likelihood ratio
NNS	Number needed to screen
NP	Nurse Practitioner
OR	Odds ratio
OSA	Obstructive sleep apnoea
PLR	Positive Likelihood ratio
PREVEND	Prevention of Renal and Vascular End-Stage Disease
QALY	Quality-Adjusted Life Year
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
RCP	Royal College of Physicians
RCT	Randomised controlled trial
ROC	Receiver operating characteristic

RR	Risk ratio
SAFE trial	Systematic screening versus routine practice for the detection of atrial fibrillation in people aged 65 and over trial
SD	Standard deviation
SROC	Summary Receiver Operating Characteristic
UI	Uncertainty interval
UK	United Kingdom
US	United states
USA	United States of America
USD	US dollar

Abstract

Background

Screening for atrial fibrillation (AF) has been recommended but is yet to be implemented in clinical practice. However, the most effective approaches for screening are not known and it is unclear if screening could feasibly be implemented in primary care.

Aims and methods

The overall aims were to determine how AF screening might feasibly and effectively be introduced into primary care in the United Kingdom (UK). Objectives were: 1) to determine the range and accuracies of methods for detecting pulse irregularities attributable to AF, 2) to determine the range and accuracies of methods for diagnosing AF using 12-lead electrocardiograms (ECGs) and 3) to investigate the feasibility and opinions of healthcare professionals (HCPs) in primary care about implementing AF screening.

Three studies were undertaken: 1) a systematic review and meta-analysis of the diagnostic accuracy of methods for detecting pulse irregularities caused by AF, 2) a systematic review and meta-analysis of the diagnostic accuracy of methods for diagnosing AF using 12-lead ECG and 3) a survey of HCPs in primary care about screening implementation.

Results

Study 1: Blood pressure monitors (BPMs) and non-12-lead ECGs had the greatest accuracy for detecting pulse irregularities attributable to AF [BPM: sensitivity 0.98 (95% CI 0.92-1.00), specificity 0.92 (95% CI 0.88-0.95), positive likelihood ratio (PLR) 12.1 (95% C.I 8.2-17.8) and negative likelihood ratio (NLR) 0.02 (95% C.I 0.00-0.09); non-12-lead ECG: sensitivity 0.91 (95% CI 0.86-0.94), specificity 0.95 (95% CI 0.92-0.97), PLR 20.1 (95% C.I 12-33.7), NLR 0.09 (95% C.I 0.06 to 0.14); there were similar findings for smart-phone applications although these studies were small in size. The sensitivity and specificity of pulse palpation were 0.92 (95% CI 0.85-0.96) and 0.82 (95% CI 0.76-0.88), respectively (PLR 5.2 (95% C.I 3.8-7.2), NLR 0.1 (0.05-0.18)].

Study 2: The sensitivity and specificity of automated software were 0.89 (95% CI 0.82-0.93) and 0.99 (95% CI 0.99-0.99), respectively; PLR 96.6 (95% C.I 64.2-145.6); NLR 0.11 (95% C.I 0.07-0.18). ECG interpretation by any HCPs had a similar sensitivity for diagnosing AF as automated software but a lower specificity [sensitivity 0.92 (95% CI 0.81-0.97), specificity 0.93 (95% CI 0.76-0.98), PLR 13.9 (95% C.I 3.5-55.3), NLR 0.09 (95% C.I 0.03-0.22). Sub-group analyses of primary care professionals found greater specificity for General Practitioners (GPs) than nurses [GPs: sensitivity 0.91 (95% C.I 0.68-1.00); specificity 0.96 (95%

C.I 0.89-1.00). Nurses: sensitivity 0.88 (95% C.I 0.63-1.00); specificity 0.85 (95% C.I 0.83-0.87)].

Study 3: 39/48 (81%) practices had an ECG machine and diagnosed AF in-house. Fewer non-GP HCPs reported having excellent knowledge about ECG interpretation, diagnosing and treating AF than GPs [Proportion (95% CI): ECG interpretation = GPs: 5.9 (2.8-12.0); healthcare assistants (HCAs): 0; nurses: 2.0 (0.3-13.9); Nurse practitioners (NPs): 11.8 (3.0-36.4). Diagnosing AF = GPs: 26.3 (17.8-37.0); HCAs: 0; nurses: 2.0 (0.3-12.9); NPs: 11.8 (2.7-38.8). Treating AF = GPs: 16.9 (9.9-27.4); HCAs: 0; nurses: 0; NPs: 5.9 (0.8-34.0)]. A greater proportion of non-GP HCPs reported they would benefit from ECG training specifically for AF diagnosis than GPs [proportion (95% CI) GPs: 11.9% (6.8-20.0); HCAs: 37.0% (21.7-55.5); nurses: 44.0% (30.0-59.0); NPs 41.2% (21.9-63.7)]. Barriers included time, workload and capacity to undertake screening activities, although training to diagnose and manage AF was a required facilitator.

Conclusions

BPMs and non-12-lead ECG were most accurate for detecting pulse irregularities caused by AF. Automated ECG-interpreting software most accurately excluded AF, although its ability to diagnose this was similar to all other HCP groups. Within primary care, the specificity of AF diagnosis was greater for GPs than nurses. Inner-

city general practices were found to have adequate access to resources for AF screening. Non-GP HCPs would like to up-skill in the diagnosis and management of AF and they may have a role in future AF screening. However, organisational barriers, such as lack of time, staff and capacity, should be overcome for AF screening to be feasibly implemented within primary care.

Chapter 1. Epidemiology of atrial fibrillation

Atrial fibrillation (AF) is the most common sustained heart rhythm disorder encountered in clinical practice and is a global public health burden. (1) Originating predominately from the left atrium, AF results in chaotic atrial activity manifesting clinically as an irregular cardiac rate and cardiac output. (2) AF is not benign and results in a hypercoagulable state predisposing to an increased risk of stroke. (3) A substantial proportion of patients with AF have no symptoms and are referred to as having asymptomatic or silent AF. (4, 5) Therefore, early detection and subsequent provision stroke preventative treatment in patients with silent AF may have significant public health benefits. (4, 5)

1.1. Incidence and prevalence of atrial fibrillation

1.1.1. Incidence and prevalence according to time and gender

The incidence and prevalence of AF have increased over time across different international healthcare systems and are both greater in men than women. A systematic review of population-based studies from 21 Global Burden of Disease regions investigated changes in the incidence and prevalence of AF between 1980 and 2010. (6) Chugh et al. identified 184 studies (no

age of inclusion restrictions applied) that were relevant to this review and estimated 33.5 million people (20.9 million men (95% uncertainty (i.e. confidence) interval (UI) 19.5-22.2) and 12.6 million women (95% UI 12.0-13.7) had AF globally in 2010. (6) In 1990, the annual age-adjusted incidence rates (95% UI) of AF were 60.7 (49.2-78.5) per 100,000 men and 43.8 per 100,000 (35.9-55.0) women. (6) By 2010 the point estimates for annual incidence rates had increased to 77.5 (65.2-95.4) and 59.5 (49.9-74.9) per 100,000 in men and women, respectively. (6) Similar trends in the point estimates for the prevalence of AF were also reported between 1990 and 2010 although, as for the reported incidence rates, the UI were overlapping; the prevalence of AF increased from 569.5 (95% UI 532.8-612.7) to 596.2 (95% UI 558.4-636.7) per 100,000 men and from 359.9 (95% UI 334.7-392.6) to 373.1 (95% UI 347.9-402.2) per 100,000 women. (6) Furthermore, Chugh et al. found that there were differences in the global distribution of AF with developed countries having a greater incidence and prevalence of AF than in developing regions. (1, 6)

A further systematic review of studies that provided up-to-date epidemiological data for the estimated incidence and prevalence of AF in European countries found the overall prevalence of AF in adults has doubled over the last 20 years. (7) Zoni-Berisso et al. reported that the current overall prevalence of AF is between 1-2%

in European countries, ranging from around 1.9% in Italy, Iceland and England, to 2.3% in Germany and 2.9% in Sweden. (7) The current population incidence of AF in Europe ranged from 0.23 per 1,000 person-years in Iceland to 0.41 per 1,000 person-years in Germany. (7)

Studies conducted within North American populations suggest the recorded incidence and prevalence of AF may be higher in the United States (US) than European countries. (8, 9) Analyses from the Framingham Heart Study suggest the recorded age-adjusted incidence of AF has increased from 3.7 to 13.4 per 1,000 person-years in men and 2.5 to 8.6 per 1,000 person-years in women between 1958 and 2007. (9) Over the same time period, the recorded age-adjusted prevalence of AF increased from 20.4 to 96.2 per 1000 person-years in men and 13.7 to 49.4 per 1,000 person-years in women. (9) This rise in prevalence over the last 50 years is likely to be due to a multiple of interacting factors over time such as improvements in diagnosis and clinical coding, changes in the prevalence of risk factors for the development of AF and improved survival from AF. (9)

Population based estimates from the far Eastern countries suggest the incidence and prevalence of AF may be lower than in Western countries, although differences in global healthcare systems and

comprehensiveness of recording clinical information may contribute to the accuracy of such epidemiological estimates. There does, however, appear to be similar trends of rising incidence and prevalence overtime as for other nations. A representative community-based study of 29,079 participants aged 30 years or older from 13 provinces in China found the population prevalence of AF, confirmed by physical examination and electrocardiography, was 0.65 per 100 people. (10) Analyses from a Chinese medical insurance database between 2001-2012 (n=471,446, 62% male, mean age 62 years) found the overall incidence of AF in adults over 20 years of age was 0.05 per 100 person-years and the prevalence of AF was 0.2 per 100. (11) The authors also found there was around a 20-fold increase in AF incidence and prevalence over the study period. (11) Studies from Japanese populations also have reported similar trends in AF prevalence. Analyses of data from periodic health examinations in 630,138 people aged 40 years and over from communities, company employees and local governments in 2003 found the prevalence of AF was 1.35 and 0.43 per 100 in Japanese men and women, respectively. (12) Moreover, Inoue et al. estimated the prevalence of AF in Japan would increase from 0.65 to 1.09 per 100 from 2010 to 2050. (12)

1.1.2. Incidence and prevalence according to age

The incidence and prevalence of AF increase with advancing age and this trend has been consistently reported from a variety of studies across different global populations and healthcare systems. (6-8, 10-24)

The prevalence of AF was estimated at around 0.12-0.5% in those under 50 years of age, 3.7%–4.2% in people between 60-70 years of age and this steeply rises to greater than 10% in the over 80 year old population. (7, 13, 16, 25)

The narrative systematic review by Zoni-Berisso et al. also suggested the incidences of AF in those aged 65–74 years were 3.2, 10.8, and 15.5 per 1,000 person-years in Scotland, Germany and the USA, respectively. (7) The incidence appeared higher in the older age group with it being reported as 6.2, 16.8, and 33.5 per 1,000 person-years in Scotland, Germany and the USA, respectively, in those aged 75–84 years. (7) These findings were consistent with analyses from Rotterdam population-based cohort study. (25) Heeringa et al. reported incidence rates of AF from 6,432 Dutch patients aged 55 years and older who had a mean follow-up of 6.9 years and found the incidence rate in those aged 55-59 years was 1.1 (95% CI 0.3–2.9) per 1,000 person-years, which increased to 20.7 (95% CI 16.8–25.3) per 1,000 person-

years in those aged 80-84 years. (25) The authors also found an increase in AF prevalence with advancing age in analyses form 6,808 participants which rose from 0.7% (95% CI 0.4–1.4) in patients aged 55-59 years to 17.8% (95% CI 14.5–21.7) in those 85 years of age and older. (25)

1.2. Risk factors for the development of atrial fibrillation

The lifetime risk of developing AF is around 20-25% in people over the age of 40 years. (11, 16, 20, 25) The point estimates for risk suggest this may be greater for men than women although the confidence around these estimates suggest the difference is likely borderline. (Men 26.0% (95% Confidence Interval (CI) 24.0-27.0) and women 23.0% (95% CI 21.0-24.0). (20)

There are a number of comorbidities that are associated with the development of AF and the European Society of Cardiology (ESC) identify increasing age, hypertension, cardiac failure, cardiomyopathies, coronary artery disease, valvular heart disease, diabetes, obstructive sleep apnoea (OSA), obesity, chronic obstructive pulmonary disease (COPD); thyroid dysfunction and chronic kidney disease (CKD) as established risk factors that associate and/or predispose to incident AF. (16-18, 22, 26-35)

Furthermore, other potential risk factors for the development of AF include asthma, (36, 37) Caucasian ethnicity, (38, 39) lower socioeconomic status, (38, 39) smoking, (40) higher levels of alcohol consumption (41) and excessive exercise. (42-45) There may also be a genetic predisposition for the development of AF. (16, 46-50)

1.3. Consequences of atrial fibrillation

AF is associated with substantial morbidity, mortality and healthcare costs, most notably from an increased risk of ischaemic stroke. (16, 51)

1.3.1. Morbidity from atrial fibrillation

The increased morbidity from AF predominately arises from symptoms of AF, the development of heart failure and AF related stroke. (52-55)

People may experience symptoms from AF, such as palpitations that arise from the characteristic feature of AF presenting with an irregular pulse, chest pain or discomfort, shortness of breath, dizziness and blackouts. (16, 51) Moreover, patients with AF also experience greater psychological distress, depressed mood (56) and impaired quality of life than those without AF and these are independent of other comorbidities. (52, 57-60)

AF is associated with a 4-5 fold increased risk of ischaemic stroke, (55) Major Adverse Cardiac Events (MACE), (61, 62) and cardiac failure. (16, 63) Strokes attributable to AF have a greater severity than non-AF related strokes. (64, 65) Moreover, prospective analyses from European and Canadian population cohorts suggest the risk of stroke from AF is greater in women than men. (66-68)

Furthermore, prospective cohort registry data suggest around 10-40% of patients are hospitalised every year with AF (52, 55, 69) and AF is independently associated with cognitive decline and vascular dementia. (52, 70, 71)

1.3.2. Mortality from atrial fibrillation

Mortality rates are approximately double in people with AF.

Analyses of prospective data from the Framingham Cohort Study found, in people aged 55-94 years (n=5,209) who developed AF during 40 years of follow-up, AF independently increased the risk of mortality (OR (95% CI) 1.5 (1.2-1.8) in men and 1.9 (1.5-2.2) in women). (72)

The Scottish Renfrew/Paisley cohort study investigated cardiovascular outcomes in 7,052 men and 8,354 women aged 45-

64 years over a 20-year period. (54) Stewart et al. found AF to be an independent predictor of all-cause mortality in both women and men (RR (95% CI) for women 2.2 (1.5-3.2) and men 1.5 (1.2-2.2). (54)

More recent analyses of cohort data over a mean 9.7 years of follow-up from 8,265 Dutch participants in the Prevention of Renal and Vascular End-Stage Disease (PREVEND) study suggested the independent risk of mortality from AF may be as much as 3-fold higher than those without AF (HR (95% CI) 3.02 (1.73-5.27)). (63)

1.3.3. Healthcare costs from atrial fibrillation

International studies across a variety of healthcare systems have demonstrated that AF is a costly public health problem, and is associated with greater healthcare utilisation and costs than in people without AF. Moreover, strokes attributable to AF incur greater healthcare costs than non-AF related strokes. (64, 65) A German study of 367 patients who were followed up for 12 months after a stroke investigated the direct hospital costs attributable to strokes and reported a greater mean direct cost per patient for those with a stroke caused by AF (€11,799 (SD 8,292) versus €8,817 (SD 7,251); p<0.001 for AF and non-AF attributable strokes, respectively). (64) Retrospective analyses of US claims data on hospital related costs from AF calculated an annual in-

patient cost of \$11,306.53 and an annual out-patient cost of \$2,826.78 per patient when the primary diagnosis was AF. (73) Moreover, another US study that also used data from a claims database estimated the incremental cost burden of undiagnosed AF at \$3.1 billion (95% CI 2.7-3.7). (74) A study in the United Kingdom (UK) investigated the projected healthcare costs directly related to AF and estimated that nearly 1% of the National Health Service (NHS) expenditure would be for AF. (75) Moreover, Stewart et al. found that approximately 50% of costs were related to hospital admissions and 20% of costs were for drug prescriptions. (75)

1.4. Symptoms, signs and diagnosis of patients with atrial fibrillation

AF results in an irregular cardiac rhythm and therefore an irregular pulse is the hallmark clinical sign of AF. (76-79) Patients with AF may present with symptoms including palpitations, shortness of breath, chest pain, lethargy, dizziness and/or syncope, (76) of which some are non-specific and may be caused by other conditions. The experience and severity of AF symptoms varies considerably between patients. The European Society of Cardiology (ESC) recommend using the Modified European Heart Rhythm Association (EHRA) symptom scale to determine the severity of symptoms in those with AF – the symptom scale ranges from 1 to

4, with 1 denoting no symptoms and a score of 4 representing disabling symptoms. (52)

An irregularly irregular pulse is usually the first clinical finding in patients with suspected AF. Once suspected, AF is diagnosed by an electrocardiogram (ECG), with a 12-lead ECG interpreted by a competent professional being recognised as the gold standard diagnostic test. (51, 52, 80)

1.5. Stroke prevention in atrial fibrillation

The prevention of stroke in patients once AF has been diagnosed is imperative to reduce the morbidity, mortality and healthcare costs associated with AF. (16, 51) Anti-thrombotic therapy to prevent AF related stroke is the only treatment that has been shown to reduce mortality associated with AF. (16)

The risk of stroke in AF is heterogeneous and increases with age, the number of AF-associated co-morbidities and is higher in women than men. (16) Patients with AF should have their risk of stroke and systemic thromboembolism calculated using the established and validated Congestive cardiac failure, Hypertension, Age ≥75 years, Diabetes and Stroke ($CHADS_2$) and/or the Congestive cardiac failure, Hypertension, Age ≥75 years, Diabetes, Stroke, Vascular disease, Age 65-74 and Sex category (CHA_2DS_2VASc)

schemata. (16, 51) The National Institute for Health and Care Excellence (NICE) and the European Society of Cardiology (ESC) recommend patients scoring ≥2 points on either risk scale should be offered stroke preventative therapies, and men with a CHA_2DS_2VASc score of 1 should be considered for such treatments. (16, 51)

Oral anticoagulation using vitamin K antagonists (VKAs), such as warfarin, has been shown to reduce the risk of stroke. A meta-analysis of 29 randomised trials (n=28,044; mean age 71 years) found, as compared to control, adjusted dose warfarin reduced the risk of stroke by around 64% (95% CI 49-74). (81) More recently direct oral anticoagulants (DOACS) have been developed and these appear to overcome difficulties in safe prescribing and monitoring of VKAs, and randomised trial evidence has found DOACS to have at least a similar efficacy for stroke prevention and similar or lower risk of haemorrhagic complications as VKAs. (82-84) Consequently, the prescription of the DOACS Dabigatran, Apixaban and rivaroxaban have been recommended, alongside the use of VKAs, for the prevention of stroke in patients with AF. (16, 51)

1.6. Silent atrial fibrillation

Patients with AF may present to healthcare professionals with symptoms as described previously. However, a substantial number

of patients with AF have no symptoms and are described as having either asymptomatic or silent AF, (16) and these terms are used interchangeably.

The EurObservational Research Programme - Atrial Fibrillation (EORP-AF) registry enrolled consecutive inpatients and outpatients, from 67 centres in nine countries that presented with AF to cardiologists. (85) Patients with AF had their symptoms scored using the EHRA symptom scale to distinguish symptom severity and impairment in daily activity. (16, 85) Analyses of data from the EORP-AF pilot registry found that, of 3,119 patients enrolled, 1,237 (39.7%) had an EHRA score of one and were therefore classified as being asymptomatic. (86) Asymptomatic patients with AF were more likely to be male, older, and have a previous history of myocardial infarction. (86) Moreover, one-year mortality was around twice higher in patients with asymptomatic AF than those with symptoms. (86)

Data from studies of pacemaker interrogation to detect silent AF suggest that asymptomatic AF may be occurring in 10.1-30% of patients with cardiac pacemakers. (87-89) However the true prevalence of silent AF may be higher or lower in unselected community populations as estimates have been derived predominately from patients in secondary care settings.

There has been an abundance of studies that have also investigated the proportion of hospital inpatients with newly detected AF after first presenting with an ischaemic stroke. Most studies within this setting have used serial ECGs or cardiac holter monitors to detect asymptomatic AF. (90-106) Up to 45% of patients presenting with stroke had undiagnosed AF although there was substantial variation in detection rates due to the method, duration and definition of AF within each study. A more recent analysis of data from 55,551 patients aged 18 years or over from a national Danish stroke registry found 9,482 (17.1%) of patients with an acute ischaemic stoke were found to have AF. (107)

Given the high prevalence of AF in asymptomatic patients and those first presenting with an ischaemic stroke, combined with the increasing prevalence of AF in an ageing population, AF and its consequences pose a significant public health burden. Early detection of AF and the subsequent provision of stroke preventative therapies could result in significant population health benefits. Consequently, screening for AF has been recommended by the European Society of Cardiology (ESC) and the Royal College of Physicians (RCP) as a method to improve the detection of AF and subsequent prevention of stroke in people over 65 years of age. (16, 80, 108)

In the following section the extent to which it would be appropriate to introduce screening for AF will be assessed and the context(s) in which this should be done.

1.7. Principles of screening programmes and applicability to atrial fibrillation screening

Published by the World Health Organisation in 1968, Wilson and Jungner identified the following 10 criteria for appraising the validity of screening programmes: (109)

1. The condition being screened for should be an important health problem.

2. The natural history of the condition should be well understood.

3. There should be a detectable early stage.

4. Treatment at an early stage should be of more benefit than at a later stage.

5. A suitable test should be devised for the early stage.

6. The test should be acceptable.

7. Intervals for repeating the test should be determined

8. Adequate health service provision should be made for the extra clinical workload resulting from screening.

9. The risks, both physical and psychological, should be less than the benefits.

10.   The costs should be balanced against the benefits.

AF screening aligns with many of the principles of screening programmes set by Wilson and Jungner. (109) As discussed in previous sections, AF is highly prevalent and an important health problem (criteria one). The natural history from the development of AF to the occurrence of thromboembolic complications is understood (criterion two). A substantial proportion of patients with AF are asymptomatic and AF is easily detectable during this early stage (criterion three). Moreover, treatments exist, are widely available and, if provided early, reduce the risk of thromboembolic complications arising from AF (criterion four). The proposed screening process, by first conducting pulse palpation (the screening test) and then diagnosing AF using ECG (the diagnostic test), is available (criterion five). However, the evidence to support screening implementation is less robust when mapped to the other screening criteria.

As AF screening fulfils many of the screening criteria, consensus from the Royal College of Physicians of Edinburgh suggested that the most cost-effective approach to detect AF in the UK is to opportunistically screen people aged 65 years or older by radial pulse palpation followed by a 12-lead ECG in those with an irregular pulse, and that this should be done in primary care. (80)

As screening aims to detect asymptomatic patients with AF prior to the development of thromboembolic complications, it is likely that non-hospital settings – such as primary healthcare and/or non-healthcare community (e.g. care homes, community health campaigns, community education groups) settings - would be the most appropriate contexts for screening implementation. However, of these two settings it is probable the primary healthcare would be the more relevant setting for AF screening. Within healthcare it is estimated that up to 90% of NHS contact occurs within primary care (110, 111) and consultation rates in GP practices are high in the elderly (111) - a group most likely to have a highest prevalence of AF. There is access to 12-lead ECG diagnosis of AF within primary care, with GP practices recording and interpreting ECGs. (112) Many patients with AF are already managed in primary care (21, 113) and, with an increasing amount of healthcare services being delivered in primary care alongside the increasing elderly population, (114) it is likely that the number of patients with AF that are managed by primary care services is set to rise. However, there have been no studies that have investigated the views of healthcare professionals in GP practices (e.g. General Practitioners (GPs) and/or nurses) about feasibly implementing AF screening and their abilities to accurately detect this arrhythmia. Indeed, understanding the views of professionals that could be expected to undertake screening would be an important priority to

ensure adequate health service provisions are in place for the extra clinical workload that would arise from screening.

Following consensus statements to implement AF screening, a review of the evidence for screening was published in 2014 for the United Kingdom (UK) National Screening Committee and the evidence was assessed against the criteria for screening programmes. (115) The review found that despite AF screening meeting many of the screening criteria there were sufficient gaps in the evidence-base to not support national implementation of an AF screening programme. The reported gaps and limitations highlighted within this report are provided below and I have mapped these to the screening criteria that were not fulfilled: (115)

- Although many approaches to screening may exist, the optimal methods for detecting and diagnosing AF were unclear (criterion five).
- An assessment of adequate staffing and facilities for the testing, diagnosis, treatment of an AF screening programme had not been undertaken. It was unclear if adequate service provision was available for the increased workload that would arise from screening implementation and, therefore, the feasibility of implementing screening was not known.

Moreover, consensus on the quality assurance measures of an AF screening had not been derived (criterion eight).

- The optimal time interval(s) for repeating AF screening and the impact of using different age thresholds for screening were not known (criterion seven).

- Treatment uptake in patients with AF was sub-optimal. Therefore, improvement in the provision of stroke preventative therapies to those with AF was needed before screening could be implemented (criterion four).

- It was unclear if people with screen-detected AF had better long-term outcomes for morbidity and mortality than those with AF diagnosed through routine care. Therefore, it was unclear if the clinical benefits from AF screening outweighed the clinical risks (criterion four).

- There was little research that investigated the views of patients, healthcare professionals and other key stakeholders about AF screening. Therefore, it was unclear whether screening was acceptable (criterion six) and if the benefits, both physical and psychological, outweighed the risks of screening (criterion nine).

- There was insufficient evidence for the cost-effectiveness of screening. Moreover, the affordability and opportunity cost of implementing screening were not established (criterion ten).

Consequently, despite the expert consensus recommendations made for AF screening in primary care, this is yet to be implemented into routine clinical practice, and research that develops our understanding of how AF screening could feasibly and effectively be introduced within primary care is warranted.

Chapter 2. Screening for atrial fibrillation

2.1. Literature review

The review in 2014 for the UK National Screening Committee did not support the implementation of AF screening and a number of gaps were highlighted in the evidence-base for this intervention when appraised against the criteria for screening programmes. (115) Research gaps included understanding better the optimal methods for detecting AF, the feasibility of implementing screening into clinical practice and translating the detection of patients with AF into improved long-term clinical outcomes.

A broad literature review was conducted with the aim of assessing the current evidence base for or against AF screening (i.e. detecting silent AF) in primary healthcare and/or community-based settings, and to further characterise the research required before screening could be introduced into routine clinical practice. A secondary aim of the review was to describe how screening was organised in studies conducted within the UK, as different contextual factors might be relevant to screening within the National Health Service (NHS).

The objectives for this review were to characterise how interventions to detect silent AF within primary healthcare and/or

community-based (i.e. non-hospital) settings have i) been organised and implemented, ii) to determine the effectiveness and/or yield of interventions to detect silent AF, iii) to determine the cost-effectiveness of interventions to detect silent AF, iv) to determine the impact on health status of patients and the acceptability of interventions to detect silent AF by patients and healthcare professionals.

2.1.1. Search strategy

The MEDLINE and EMBASE databases were searched for studies until January 2016 using the following Medical Subject Headings (MeSH) terms, keywords and associated wildcard terms:

- Atrial fibrillation
- Atrial flutter
- Auricular fibrillation
- Irregular pulse
- Irregular heart
- Irregular rhythm
- Screening
- Mass screening
- Detect
- Identify

The National Institute for Health Research (NIHR), European Society of Cardiology (ESC) and Royal College of Physicians (RCP) guidelines, the Cochrane Library, Cochrane Controlled Trials Register, and the AF Screen International Collaboration were also searched.

Using a systematic search strategy, studies were included that were published in English and addressed the topic of detecting silent AF in adults aged 18 years or over in non-hospital settings. Studies were included that recruited participants from primary healthcare (e.g. GP practices, pharmacies, opticians), non-healthcare community (e.g. care homes, community health campaigns, community education groups) and/or outpatient clinic settings. Outpatient clinic settings were included in the definition of non-hospital settings as outpatient services are increasingly being delivered out of hospitals and studies within this setting may be translatable to the delivery of screening in primary care. Studies conducted using hospital inpatients or in emergency care settings were not included. Empirical research studies of any study design, with the exception of case reports and case series, that reported clinical outcomes (e.g. number of new cases of AF, stroke risk in those with new AF, number of strokes after AF detection, harms from the treatment of AF) for the effectiveness and/or yield, cost-effectiveness, impact and/or acceptability on patients or healthcare

professionals from AF screening interventions were included. Effectiveness was defined as clinical outcomes from interventions to detect silent AF when compared to other interventions or routine care. Yield was defined as clinical outcomes from interventions to detect silent AF when there were no comparator groups in studies. Review articles were also eligible for inclusion. Studies that investigated intensive methods of detecting silent AF after an acute stroke (e.g. cardiac holter monitoring, implantable reveal devices) were not reviewed as these are not translatable to mass screening of asymptomatic patients in the general population.

The titles and abstracts of potentially relevant papers were initially screened (by JT) and only studies felt likely to meet the inclusion criteria were obtained for full-text review. The reference lists of review articles were also screened for relevant citations.

2.1.2. Analyses

Studies were grouped and data extracted under the relevant themes of i) how interventions to detect silent AF were organised and implemented, ii) the clinical effectiveness and/or yield and iii) cost-effectiveness of interventions to detect silent AF, and iv) the impact on health status of patients, and acceptability of AF screening by patients or healthcare professionals. The description of studies and outcomes were narratively reported.

2.2. Results

2.2.1. Study characteristics

The database search identified 2,229 citations and, after removal of duplicate records, there were 1,927 citations for further assessment. After considering titles and abstracts there were 55 potentially relevant articles that were extracted for full-text review. Subsequently, 30 articles met the selection criteria and were included in the final literature review. These included two systematic reviews, (116, 117) three randomised controlled trials, (118-121) one secondary analysis of trial data, (122) and 20 uncontrolled studies of case finding from AF screening interventions. (35, 123-141) Another two studies exclusively reported economic analyses from AF screening interventions (142, 143) and one study exclusively reported outcomes for the acceptability of AF screening by patients and healthcare professionals. (144) Of the 20 uncontrolled studies of AF case finding, there were two studies that retrospectively analysed baseline cohort data for new diagnoses of AF in participants. (128, 135) Therefore, these two studies were not designed *a priori* as AF screening intervention studies.

Of the individual studies (i.e. non-systematic reviews) identified by the literature search, 10 were conducted in Europe, (35, 121, 123, 124, 126, 127, 129, 138, 139, 142) 8 in the UK, (118-120, 122,

130, 131, 137, 141) 5 in the US, (128, 132, 133, 135, 136) 4 in Australia or New Zealand (125, 134, 140, 144) and one in Japan. (143)

2.2.2. Organisation and implementation of interventions to detect silent atrial fibrillation

2.2.2.1. Process of atrial fibrillation detection within studies

Two processes for detecting silent AF were identified – systematic and opportunistic detection. Most studies investigated a systematic approach for detecting AF (invitation of all people within a target population at risk of AF) as the method for detecting new cases of AF. (35, 118-121, 123, 125, 127, 128, 130, 131, 133, 135, 137-139, 141) Fewer studies used opportunistic case detection of AF where participants were usually opportunistically screened for AF during encounters with healthcare professionals for other reasons. (118-120, 124, 126, 129, 132, 134, 136, 140)

Only two studies were found that directly compared outcomes from the systematic and opportunistic processes of AF detection, (118-120) both of which were randomised trials conducted in the UK. The remaining UK studies investigated systematic approaches to AF detection. (130, 131, 137, 141)

2.2.2.2. Periodicity of detecting silent atrial fibrillation within studies

There were two periodicities (i.e. frequencies of attempts made) for detecting new cases of AF within studies – multiple intermittent attempts made prospectively to detect AF made over a defined time-period (121, 127, 129, 139) or only one attempt in total for AF detection. (35, 118-120, 123-126, 128, 130-135, 137, 138, 140, 141)

Of the studies that used an intermittent approach for detecting AF, two used twice-daily ECG recordings made every day over a two week period, (127, 139) one used twice-daily ECG recordings made every day over four weeks, (129) and another used patient self-assessment for pulse irregularities once every month and then six-monthly clinical assessments by healthcare professionals, including 12-lead ECG, over a total study duration of two years. (121)

Of studies using single time-point AF detection there were two further methods used to identify silent AF. Studies used either a recording of one ECG to detect AF ('one-step' method) (35, 118-120, 123-125, 128, 130-132, 134, 135, 141) or firstly identifying pulse irregularities before performing a diagnostic ECG in those with suspected AF ('two-step' method). (118-120, 126, 133, 136-138, 140)

The majority of studies that used the one-step approach for single time-point screening used 12-lead ECG, (35, 118, 119, 125, 128, 130, 135, 141) and others used single-lead ECG, (120, 124, 132, 134) three-lead ECG, (123) four-lead ECG, (131) and/or seven-lead ECG (135) for detecting silent AF.

The studies that used a two-step approach used pulse palpation (118-120, 136-138) and/or single-lead ECG (126, 133, 140) for the first-step of identifying those with suspected AF. For the second-step of confirming AF nearly all studies used 12-lead ECG, (118, 119, 126, 133, 137, 138, 140) whilst one used single-lead ECG, (120) and another used self-reported outcomes from self-referral to a medical practitioner after an irregular pulse was identified. (136)

All of the UK studies used the single time-point approach for detecting silent AF. (118-120, 130, 131, 137, 141) The majority of these used the one-step method of screening using an ECG. (118-120, 130, 141) Others used a two-step method of pulse palpation followed by ECG confirmation of AF. (118-120, 137)

2.2.2.3. Healthcare settings and professionals used to detect silent atrial fibrillation

Most studies of interventions for the detection of silent AF were conducted in family/GP practices and involved their practice staff (such as GPs and/or nurses) for conducting screening activities. (118-120, 123, 124, 130, 131, 137, 138, 141) Three studies involved patient self-recording of ECGs (127, 129, 139) and two studies were conducted in pharmacies and involved pharmacists undertaking screening activities. (134, 140)

For the vast majority of studies a trained cardiac specialist interpreted ECGs to make the final diagnosis of AF. (35, 118-120, 123, 125-127, 129, 131-135, 137, 139-141) Two studies used automated analysis (124, 128) and one study used only family physician interpretation of ECGs for AF diagnosis. (138)

All UK studies were conducted in GP practices and involved practice staff, mostly GPs and/or nurses, undertaking screening activities. (118, 119, 130, 131, 137, 141)

2.2.2.4. Selection of participants within silent atrial fibrillation detection studies

For the studies that investigated systematic detection of AF, most identified participants through either random (35, 118-121, 123,

128, 135, 139) or total population sampling. (125, 127, 130, 131, 133, 138, 141) Random selection of participants was from either patient lists at primary healthcare centres and/or GP practices (118-121, 123) or lists of community residents. (35, 128, 135, 139) Total population sampling of participants was from all eligible people at primary healthcare centres and/or GP practices, (130, 131, 138, 141) all inhabitants of communities, (127, 133) or all attendees at an outpatient clinic. (125) One study systematically screened all patients ≥65 years of age that attended an influenza clinic within primary care in the UK. (137)

Within studies of opportunistic AF detection, participants either self-selected to participate or were screened opportunistically when consulting healthcare professionals about other health problems. (118-120, 124, 126, 129, 132, 134, 136, 140) Participants were opportunistically identified within primary care medical centres and/or outpatient clinics, (118-120, 124, 126, 129, 132) community pharmacies, (134, 140) and one study detected silent AF in people that attended an education group about AF. (136) All of the UK studies that investigated opportunistic approaches to screening were undertaken in primary healthcare settings.

2.2.2.5. Age of participants within silent atrial fibrillation detection studies

The range of age thresholds for including participants in studies of detecting silent AF was broad. The majority of studies included all people ≥65 years old. (118-121, 123, 127, 128, 130, 131, 134, 137-139, 141) Of these studies, there were two that included participants between 75-76 years of age (127, 139) and one included those ≥70 years old. (123)

One study included people ≥55 years of age. (140) The age of inclusion for the remaining studies were ≥45 years, (135) ≥40 years, (124, 125, 132) 35-75 years, (35) ≥18 years, (126) and 12-99 years. (133) All studies conducted in the UK setting included participants ≥65 years of age. (118-120, 130, 131, 137, 141)

2.2.2.6. Summary for the organisation and implementation of interventions to detect silent atrial fibrillation

Most studies of interventions to detect silent AF were conducted in primary healthcare settings. Two processes – systematic and opportunistic screening – were identified for detecting silent AF. The majority of studies investigated the detection of AF in people ≥65 years of age and investigated AF detection at a single-time point. There were two subsequent approaches for detecting AF; the one-step approach where AF was directly diagnosed using ECGs, or

the two-step approach where an irregular pulse were firstly identified and then diagnostic ECG performed in those with suspected AF.

All UK studies were conducted in GP surgeries, involving practice staff, and screened for AF in patients ≥65 years of age. All studies investigated single-time point screening, using either a one or two-step approach to screening.

2.2.3. Clinical effectiveness and/or yield of interventions to detect silent atrial fibrillation

There were 27 studies that reported outcomes for the clinical effectiveness and/or yield of interventions to detect silent AF – two systematic reviews, (116, 117) three randomised trials (reported across four articles), (118-121) 20 uncontrolled studies of AF case detection, (35, 123-141) and one secondary analysis of randomised trial data. (122)

The clinical effectiveness and/or yield of interventions was primarily reported as the number of new cases/proportion of AF detected, incident AF and/or screen-detected AF. Some studies also reported the risk of stroke in patients with screen-detected AF using the established $CHADS_2$ and/or CHA_2DS_2VASc risk stratifying schemata; consequently, these studies also provided data for the

51

effectiveness and/or yield of screening interventions to detect AF cases that could also be eligible for stroke preventative treatment. Only one study provided data for longer-term clinical outcomes arising from the treatment of those with new AF. Within this section, all such clinical outcomes (i.e. screen detected AF, stroke risk scores and longer-term clinical outcomes) arising from interventions to detect silent AF have been provided under the domain of clinical effectiveness and/or yield and have been reported together for the individual studies that provided such data. The following sections provide information for the clinical effectiveness and/or yield of interventions to detect silent AF according to study design - notably systematic reviews, randomised trials, secondary analyses of randomised trial data and uncontrolled studies of AF case finding.

2.2.3.1. Systematic review evidence for the clinical effectiveness and/or yield of interventions to detect silent atrial fibrillation

Individual studies that were included in the two systematic reviews, that also met the selection criteria for the current literature review, have been individually appraised in subsequent sub-sections of this chapter. However, where relevant the point estimates for clinical outcomes (as defined above) from the two

systematic reviews that are not reported within individual studies have been provided in this sub-section.

One of the systematic reviews was a Cochrane review of randomised trials, controlled before and after, and interrupted time series studies that investigated the effectiveness of AF screening programmes for the detection of new AF when compared to routine practice. (117) Only one randomised trial met the selection criteria for the Cochrane review and this study has been appraised in the following sub-section of chapter two. (117-119)

The other systematic review investigated the prevalence of AF and incidence of unknown AF from studies of single time-point screening in ambulatory populations using either ECG or pulse palpation. (116) The review identified 31 studies (26 prospective cohort studies, two retrospective cohort studies and two randomised controlled trials) from nine countries that included 122,571 patients (mean age 64 years, 54% male).

There was an attrition of included studies with data to enable calculation of point estimates for the incidence of new AF from interventions to detect silent AF. Many of the studies were uncontrolled studies of AF case finding and these have been described in greater detail in the subsequent section of this chapter. (116) Overall, the incidence of previously undiagnosed AF

from interventions [14 studies, n=67,772] was 1.0% (95% CI 0.89-1.04). Sub-group analyses determined the incidence of undiagnosed AF from studies conducted in both GP/outpatient clinics, non-healthcare related community settings (e.g. screening from community advertisements or population screening) and in people ≥65 years of age. The incidence of new AF was higher in studies conducted within a GP/outpatient clinic setting [5 studies (n=13,533)] than other non-healthcare related community settings [8 studies; n=54,239; 1.2% versus 0.9% (p<0.001)]. Furthermore, the incidence of AF was greatest at 1.4% (95% CI 1.2–1.6%) when analyses were restricted to studies that included participants ≥65 years of age (8 studies, n=18,189). (116)

Secondary outcomes of this review were to determine the stroke risk scores and eligibility for oral anticoagulation in those with new AF. Four studies (n=5,676) reported outcomes for anticoagulation eligibility but only two of these reported $CHADS_2$ or CHA_2DS_2VASc scores; (125, 127) point estimates for the risk of stroke in those with new AF were not calculated in this systematic review. However, the two studies that provided stroke risk scores have been included in the current literature review and their clinical outcomes are provided in subsequent sections of this chapter.

Although this systematic review included more studies than the Cochrane review, these were of various and weaker designs, and the review aggregated data mostly from uncontrolled studies of AF case finding. Consequently, this increases the risk of bias when determining point estimates and the findings from this review mostly provide data for the yield of interventions to detect undiagnosed AF.

2.2.3.2. Randomised trial evidence for the clinical effectiveness of interventions to detect silent atrial fibrillation

Three randomised trials investigated the effectiveness of interventions to detect incident AF and all were conducted in primary healthcare settings. (117-121) Two were conducted in the UK (118-120) and one is Spain. (121) One trial compared the effectiveness of two interventions with usual care whilst also providing a comparison of the effectiveness between the two interventions. (117-119) Another trial only compared the effectiveness of an intervention with usual care, (121) and the remaining trial only compared the effectiveness of two interventions with one other. (120)

2.2.3.2.1. Randomised trial evidence for the clinical effectiveness of interventions to detect silent atrial fibrillation compared to usual care

The largest trial of detecting silent AF was the systematic screening versus routine practice for the detection of atrial fibrillation in people aged 65 and over (SAFE) study. (117-119) This cluster-randomised trial set within primary care recruited patients ≥65 years of age across 50 practices in England, UK. This three-arm trial compared two single time-point AF detection interventions with AF detection arising from usual care. (117-119) Practices within the intervention arms of the study (n=25) were randomly allocated to implement either systematic screening (systematic invitation to all patients for the one-step approach of ECG recording) or opportunistic screening (two-step approach of checking for an irregular pulse with confirmatory ECG, as required) by GPs and/or nurses. (117-119) The study recruited 14,802 patients (mean (SD) age 75.3 (7.2) years; 42.6% male) that were equally distributed across each study arm. (117-119) The overall detection rate of new cases of AF was 1.63% a year in the intervention practices and 1.04% in control practices (difference 0.59%; 95% CI 0.20-0.98). (118, 119) Compared to usual care, systematic screening was 57% [OR 1.57 (95% CI 1.08-2.26)] more likely to detect incident AF; similarly, opportunistic screening was 58% [OR 1.58 (95% CI 1.10-2.29)] more likely to detect

incident AF than usual care. (117) Consequently, the number needed to screen (NNS) to detect one additional case of AF was 172 (95% CI 94-927) for systematic screening and 167 (95% CI 92-806) for opportunistic screening when compared to routine practice. (117)

Another randomised trial set within primary care in Spain investigated the effectiveness of a two-year AF detection programme. (121) Randomly selected patients, with at least one risk factor for AF (age ≥65 years, hypertension, ischaemic heart disease, valvular heart disease, diabetes and/or congestive cardiac failure) were invited to participate from an urban primary healthcare centre. Excluded participants included those with pacemakers and those unable to attend the health centre. Participants (n=928) were randomised to receive either a screening intervention or usual care (the control group) for detecting new AF. (121) The intervention was intermittent screening and comprised, after instruction by a trained nurse at the baseline visit, monthly patient self-assessment for pulse irregularities, and six-monthly healthcare professional assessments of a full medical history, physical examination and an ECG. (121) The primary outcome for this trial was newly diagnosed AF at 6 months and secondary outcomes included patients diagnosed with AF at 2-years follow-up and the complications arising from AF and its treatment. (121) At

six-months follow-up more cases of new AF were detected in screened participants than from usual care (8 (1.7%) versus 1 (0.2% cases; p=0.018). (121) At two-years there were similar rates of new AF detection in both trial arms (11 (2.5%) intervention versus 6 (1.3%) usual care; p=0.132). (121) Time to first diagnosis of AF was shorter in the intervention group (median (IQR) time to diagnosis 7 (192) days versus 227 (188.5) days for the intervention and controls groups, respectively; p=0.029).

The risk of stroke for patients with new AF were not reported but at two years 90.9% of patients with new AF had at least two risk factors for stroke in the intervention group as compared to 66.7% of controls. (121)

At two years of follow-up 10/11 patients with new AF in the intervention group were started on anticoagulation therapy compared to 2/6 patients in the control group. Only two patients were reported to have mild treatment related complications, one patient from each trial group. (121)

2.2.3.2.2. Randomised trial evidence comparing the clinical effectiveness of systematic and opportunistic approaches of interventions to detect silent atrial fibrillation

The SAFE study, described previously, also compared as part of its primary study design the effectiveness of systematic and opportunistic screening for detecting new cases of AF. (117-119)

This found that both approaches for screening detected similar numbers of new cases of AF (1.62% v 1.64%, respectively; difference 0.02%, −0.5% to 0.5%). (117-119)

The third randomised trial of AF screening included 3,001 patients aged 65-100 years from four general practices within the Medical Research Council (MRC) general practice framework, UK. (120) Patients were randomised to single time-point AF detection of either systematic nurse-led screening (systematic invitation for patients to attend for pulse palpation and a single-lead ECG) or opportunistic case finding for AF (prompts entered into patient notes to conduct two-step screening that comprised a pulse check during consultations with healthcare professionals and then undertake single-lead ECG if appropriate). (120) There was no trial arm to determine AF detection from routine practice. There was a greater detection of any AF in systematic screened patients (n=67; 4.5%) compared to those exposed to opportunistic case finding (n=19; 1.3%); OR (95% CI) 3.7 (2.2-6.1). The yield of new AF was lower with 12 (0.8%) new cases of AF in the systematic screening arm and seven (0.5%) in the opportunistic case-finding arm. It was estimated that the NNS to detect one case of AF was 31 (95% CI 23-50). (120) This trial also found that 47/67 (70%, 95% CI 58-81) patients with AF that were identified by systematic screening had, other than AF, at least one other risk factor

(previous stroke or transient ischaemic attack, hypertension or diabetes) for stroke. (120) Combined with the age threshold of ≥65 years for inclusion of patients into this study, one can reasonably assume the majority of patients with AF detected in this trial would have had a risk score sufficiently high to warrant further stroke preventative treatment.

2.2.3.2.3. Secondary analyses of randomised trial evidence comparing the clinical effectiveness of systematic and opportunistic approaches of interventions to detect silent atrial fibrillation

A secondary analysis of the SAFE trial data was conducted and reported the risk of stroke, using baseline trial data, in those diagnosed with new AF from the intervention practices. (122) As baseline data to enable the calculation of stroke risk were not available for patients in the control arm there was no comparison of stroke risk in patients with screen-detected AF and those with AF detected through routine practice. (122) The majority of patients with screen-detected AF had a $CHADS_2$ score≥1 and there were no significant differences in the proportions of patients with these scores between the two intervention arms (Proportion (95% CI) with $CHADS_2$ scores≥1 82.7% (72.6-89.6) and 78.4 (67.7-86.2); p=0.51 in the opportunistic and systematic screening arms, respectively). (122) There were also a substantial proportion of

patients with CHADS$_2$ scores≥2 (Proportion (95% CI) with CHADS$_2$ scores≥2 29.3% (20.2-40.4) and 43.2% (32.6-54.6); p=0.077 in the opportunistic and systematic screening arms, respectively). (122)

2.2.3.3. Uncontrolled studies of atrial fibrillation case detection

There were 20 uncontrolled case finding studies for the detection of silent AF. (35, 123-141) These studies have been described in chronological order to enable appreciation of any changes in study design over time and are summarised in table 2-1.

There were two studies that reported AF detection as part of baseline data collection within a cohort study (128, 135) and, therefore, these studies have limited applicability to screening than the other case finding studies, as they were not designed *a priori* to screen for silent AF.

Most studies used single time-point screening to detect AF; (35, 123-126, 128, 130-138, 140, 141) eleven studies used a one-step approach of recording an ECG to detect AF, (35, 123-125, 128, 130-132, 134, 135, 141) six used two-step screening of firstly identifying an irregular pulse with confirmatory ECG in those with suspected AF. (126, 133, 136-138, 140) The remaining three

studies used intermittent screening at multiple time-points. (127, 129, 139)

It appears that more recently non-12-lead ECGs, particularly single-lead ECG, have been used more often to detect AF than in earlier studies of AF detection. (127, 129, 131, 133, 139, 140) Moreover, recent studies have investigated the yield of intermittent screening using single-lead ECG over multiple time-points to detect AF. (127, 129, 139) Consequently, there appears to be greater prominence on using non-12-lead ECGs for detecting suspected AF than other approaches, such as pulse palpation, in more recent studies.

No studies provided comparative estimates for the number of AF cases detected from routine clinical practice or usual care. Only eight of these studies provided data for the stroke risk in patients with newly diagnosed AF. (35, 123, 125, 127, 129, 134, 137, 139) Therefore, these studies only provide data for the yield of clinical outcomes from interventions to detect silent AF.

All studies showed to a variable extent that undiagnosed AF exists and interventions to detect silent AF, irrespective of method used, were able to identify new cases of AF. The yield of new AF detection from the uncontrolled studies ranged from 0.2-9.0% although the majority of studies reported at least 1.0% new AF

detection. The studies that reported stroke risk scores suggest the likelihood of treating those with new AF would affect clinical outcomes. No studies provided data for longer-term clinical outcomes, such as changes in stroke burden or complications from treatment.

There were only four UK studies of uncontrolled AF case finding. (130, 131, 137, 141) Three studies only provided data for new cases of AF detected. (130, 131, 141) All UK studies were conducted in GP surgeries and investigated systematic AF detection in patients ≥65 years of age. Three used the one-step method of identifying AF at a single time-point. (130, 131, 141) The yield of patients with new AF in UK studies ranged from 0.3-1.2%.

Many of the uncontrolled studies had low response rates from people that were invited to participate in screening and this is a source of non-response bias in their findings. Combined with the uncontrolled study design the findings from these studies have limited utility beyond understanding the potential methods that could be used for AF screening.

Table 2-1: Uncontrolled studies of interventions to detect silent atrial fibrillation

Study	Country	Setting & HCPs involved [a]	Age	Screening process	Method of AF detection	Number screened (n)	RR (%) [b]	New AF (%) [c]	Stroke risk: [d] (CHADS$_2$/ CHA$_2$DS$_2$VASc)
Hill 1987 (130)	UK	GP surgery (n=1); nurses	≥65	Systematic: Single time-point	One step: 12-lead ECG	819	80.7	1.2	n/a
Furberg 1994 (128)	USA	Community (Cohort study); n/r	≥65	Systematic: Single time-point	One step: 12-lead ECG	5,151	n/r	1.5	n/a
Lavenson 1998 (132)	USA	Community (outpatient clinic); n/r	>40	Opportunistic: Single time-point	One step: Single lead ECG or apical pulse auscultation	176	n/r	9.0*	n/a
Wheeldon 1998 (141)	UK	GP surgery (n=1); technician	≥65	Systematic: Single time-point	One step: 12-lead ECG	1,207	84.9	0.4	n/a
Munchauer 2004 (136)	USA	Community (281 group education sessions); n/r	>50	Opportunistic: Single time-point	Two step: Pulse palpation +/- self referral for healthcare professional assessment	1,839	42.5	0.5	n/a
Doliwa 2009 (126)	Sweden	Community (publically attended	≥18	Opportunistic: Single time-point	Two step: Single lead ECG +/- 12-	606	n/r	1.0	n/a

		ESC congress); self-recorded			lead ECG				
Meschia 2010 (135)	USA	Community (Cohort study); n/r	≥45	Systematic: Single time-point:	One step: 12-lead or 7 lead ECG	29,861	49	0.6	n/r
Claes 2012 (124)	Belgium	Primary care medical centres (n=69); nurses	≥40	Opportunistic: Single time-point	One step: Single lead ECG	10,758	n/r	1.6	n/r
Schnaebel 2012 (35)	Germany	Community; n/r	35-75	Systematic Single time-point	One step: 12-lead ECG	5,000	64.0	0.5	2.0/3.0
Deif 2013 (125)	Australia	Out-patients (retrospective analysis of pre-surgical ECGs); n/r	≥40	Systematic: Single time-point	One step: 12-lead ECG	2,808	n/r	All ages: 0.4 ≥65 years: 0.6	All ages: 1.9 (1.5)/3.3 (2.2) ≥65 years: 2.2 (1.5)/3.8 (2.0)
Sanmartain 2013 (138)	Spain	Primary care medical centres (n=3) & out-patients (n=1); nurses	≥65	Systematic: Single time-point	Two step: Pulse palpitation +/- 12-lead ECG	1,532	17.3	1.1	n/r
Hendrikx	Sweden	Family	n/r	Opportunistic:	Intermittent:	928	93.6	3.8 (2.7-	2 (1-4) / -

2013 (129)		practices (n=8) & out-patients (n=2); self-recorded		Multiple time-points	Single lead ECG twice daily over 4 weeks			5.2)	
Rhys 2013 (137)	UK	GP surgery (n=1); nurses and GPs	≥65	Systematic: Single time-point	Two step: Pulse palpation +/- 12-lead ECG	573	33.4	0.3	- / 5
Engdahl 2013 (127)	Sweden	Community; self-recorded	75-76	Systematic: Multiple time-points	Intermittent: Twice daily single lead ECG recording over 2 weeks	403	47.5	7.4 (5.2-10.4)	2.5 / -
Walker 2014 (140)	New Zealand	Pharmacy; (n=1); pharmacists	≥55	Opportunistic: Single time-point	Two step: Single-lead ECG +/- 12 lead ECG	121	n/r	1.7	n/r
Javed 2014 (131)	UK	GP surgery (n=15); practice staff	≥65	Systematic Single time-point	One step: Four lead ECG	6,856	30.7	0.8	n/r
Lowres 2014 (134)	Australia	Pharmacy (n=10); pharmacists	≥65	Opportunistic: Single time-point	One step: Single lead ECG	1,000	n/r	1.5 (0.8-2.5)	3.7 (1.1) / -
Bury 2015 (123)	Ireland	GP surgery (n=25); practice staff	≥70	Systematic: Single time-point	One step: Three-lead ECG	566	56.4	2.1	- / 4 (1-7)

Le Page 2015 (133)	US	Community (hospital foyer); doctors and nurses	12-99	Opportunistic: Single time-point	Two step: Single-lead ECG +/- 12 lead ECG	954	n/r	0.2	n/r
Svennberg 2015 (139)	Sweden	Community; self-recorded	75-76	Systematic: Multiple time-points	Intermittent: Twice daily single lead ECG recording over 2 weeks	7,173	53.8	3.0 (2.7-3.5)	3.5 (1.2) / -

n/r = Not reported; *study only reported proportion of arrhythmias detected and new AF not specified; [a] = setting from which participants were recruited (community settings refer to non-healthcare settings in the community; out-patients refers to hospital based out-patient clinics; GP surgery refers to General Practices and HCPs refers to healthcare professionals involved in screening; [b] = RR (Response rate) is the number of people screened from those invited for screening; [c] = Proportion (95% CI) of new cases of AF identified by the intervention; [d] = Values presented as means (SD), with the exception of Hendrikx 2013 and Bury 2015 where median (IQR) stroke risk scores are provided

2.2.3.4. Summary of studies for the clinical effectiveness and/or yield of interventions to detect silent atrial fibrillation

2.2.3.4.1. Detecting new cases of atrial fibrillation

There were two systematic reviews and three randomised trials that reported clinical outcomes for the detection of new AF. Data from one systematic review and two randomised trials (one of which was the only study in the systematic review) suggest that AF screening, as compared to routine practice, is likely to be effective at detecting new cases of AF. It remains unclear which interventions have the greatest effectiveness for detecting AF when compared to one another. However, the largest trial of AF screening interventions, the SAFE trial, suggested that there is no difference between systematic and opportunistic processes of AF screening for the detection of new AF.

Most evidence for the ability of interventions to detect new cases of silent AF has been derived from uncontrolled studies of AF case finding. These studies suggest that undiagnosed AF exists and that screening interventions detect silent AF to a variable extent. The other systematic review, which mostly included uncontrolled case finding studies, suggested the yield of AF case finding may be greatest in those aged ≥65 years old and when conducted in primary healthcare settings.

2.2.3.4.2. Risk of stroke in new cases of atrial fibrillation

Of the studies that reported stroke risk scores for patients with incident AF, most calculated the risk using either the $CHADS_2$ and/or CHA_2DS_2VASc risk stratifying schemata. Patients with screen-detected new AF have stroke risk scores sufficiently high to justify the subsequent treatment of AF using stroke preventative therapies. However, most studies that reported the risk of stroke in patients with screen-detected AF did not provide a comparison of the stroke risk in those with AF detected from usual care.

2.2.3.4.3. Long-term clinical outcomes in new cases of atrial fibrillation

The literature review found only one study that reported long-term clinical outcomes from the treatment of those with newly diagnosed AF; this study found minor adverse effects arising from the treatment of those with screen-detected AF and outcomes were similar in those with AF diagnosed and treated from routine practice. However, there was a clear lack of evidence for longer-term clinical outcomes arising from the treatment of patients with screen-detected AF, such as the progression of AF, changes in stroke burden and/or consequences of stroke preventative treatments.

2.2.4. Cost-effectiveness of atrial fibrillation screening

There were seven articles that reported economic analyses from six studies of AF screening; data were reported from two randomised trials, (119, 120) three uncontrolled case finding studies (134, 137, 139, 142) and one modelled economic analyses using simulated epidemiological data. (143)

The SAFE study, the largest RCT of AF screening, reported outcomes from within trial and model based economic analyses. (119) From an NHS only perspective the within trial analyses found, compared to no screening (i.e. routine care), the overall incremental costs for detecting new cases of AF within opportunistic and systematic screening trial arms were £9,429 and £40,882, respectively. As the number of new AF cases detected were similar in both intervention arms, opportunistic screening provided greater cost-effectiveness than systematic screening; the Incremental Cost-Effectiveness Ratio (ICER) for opportunistic screening was of £337 per additional new case of AF detected; this assumed an acceptable Incremental Cost-Effectiveness Ratio (ICER) per additional case of AF being set at this value. (119) Using both NHS and patient costs, the incremental cost of detecting an additional case of AF increased to £363 from opportunistic screening yet this remained the more cost-effective approach than systematic screening. (119) A number of model-based analyses were conducted that evaluated the effects of

screening on long-term consequences arising from the treatment of those with screen-detected AF, and the impact of different screening configurations for detecting AF. (119) Compared to routine care, opportunistic screening increased the percentage of people with newly detected AF which was most marked by annual screening. Combined with the effects of stroke risk reduction and complications arising from treatment, economic modelling suggested opportunistic AF screening would at worst be cost-neutral and at best produce a small reduction in overall costs. (119)

The other RCT compared the effectiveness of systematic nurse-led screening with opportunistic case finding of AF but only provided data for within trial economic analyses from the systematic screening intervention arm. (120) Comparisons for the cost-effectiveness of systematic with opportunistic screening were not reported. (120) As a result of systematic screening, one additional patient with atrial fibrillation was detected for every 31 screened (95% CI 23-50) and, using a cost estimate of £6 per consultation with a practice nurse, the reported cost per atrial fibrillation case detected of £186 (95% CI = £138 to £300). (120) The number needed to screen to detect a new case of AF was 91 with a minimum cost estimate per case identified (based on practice

nurse time) at £550 but confidence around these estimates were not reported. (120)

A smaller uncontrolled study by Rhys et al. provided estimates for the cost of systematic screening during influenza clinics. (137) The authors reported the cost of identifying a new case of AF as approximately £234 and estimated the total annual cost to prevent one stroke using oral anticoagulation as approximately £9,911. (137) However, the authors did not conduct further economic analyses for cost-effectiveness beyond the estimation of incurred screening costs. (137)

Economic analyses were also reported from the search-AF study – an uncontrolled study of AF detection using single-lead ECGs at community pharmacies in Australia. (134) Assuming a 50% screening participation rate and 55% treatment adherence, opportunistic screening using single-lead ECGs was associated with an Incremental Cost-Effectiveness Ratio (ICER) per Quality-Adjusted Life Year (QALY) gained of $AUD 5,988 (95% CI 1,613-13,435) [€3,142; $USD 4,066]. The ICER per stroke avoided was $AUD 30,481 (95% CI 8,210-68,384) [€15,993; $USD 20,695]. (134) Lowres et al. reported that opportunistic screening using this approach to AF screening was cost-effective. (134)

Two studies reported economic analyses from the STROKE-STOP study. (127, 139) The uncontrolled STROKE-STOP study investigated silent AF detection using intermittent ECG recording over two weeks. Within trial analyses suggested this approach to AF detection was associated with a cost of €4,164 per QALY gained. (139) Subsequent economic analyses using the STROKESTOP data and a simulated Markov model for 1,000 patients assessed cost-effectiveness. (142) Aronsson et al. found that this approach to screening would result in eight fewer strokes, 11 more life-years, and 12 more QALYs per 1,000 population screened. (142) Moreover, this approach to screening resulted in an incremental cost of €50,012, a cost of €4,313 per QALY gained and €6,583 per avoided stroke. (142) The authors concluded that systematic AF screening using intermittent ECG recording was cost-effective assuming the willingness to pay around €5,000 per QALY gained. (142)

Maeda et al. reported their findings of a simulated analysis that used epidemiological data from the Framingham Study data and applied this to a hypothetical population of Japanese patients receiving healthcare from the ages 65-85 years. (143) Using a Markov model, Maeda et al. compared the cost-effectiveness of annual screening using either systematic ECG recording or pulse palpation followed by ECG in those with an irregular pulse, with no

screening. (143) The authors found that both screening approaches were similar in effectiveness and cost-effectiveness. The ICERs in males and females per QUALY were $8,000 and $10,000, respectively. Medea et al. concluded that both approaches to screening were feasible and cost-effective for the prevention of stroke. (143)

In summary, research data suggests AF screening may be cost-effective and randomised trial data suggests the more cost-effective approach is opportunistic AF case detection. Data from uncontrolled case finding studies provide information about the incurred costs of AF detection; these studies suggest detecting silent AF could be cost-effective but assume the costs incurred are acceptable to healthcare providers. The uncontrolled studies, however, do not provide comparative estimates of the costs of detecting AF that would have occurred from routine practice. Furthermore, none of the studies reported modelled outcomes for the affordability of AF screening when delivered at a population level. Although AF screening may be cost-effective, the overall costs to healthcare systems and providers could potentially be large and deemed uneconomical when considered alongside the delivery of equitable population health.

2.2.5. Impact on the health status of patients and acceptability of detecting silent atrial fibrillation by patients and healthcare professionals

Despite the large number of studies investigating the clinical effectiveness and/or yield of interventions for detecting silent AF, there were few studies that reported outcomes about the impact and/or acceptability of AF detection for patients and/or healthcare professionals. Only four studies reported outcomes for the impact, acceptability, opinions and/or training requirements about AF screening by patients or healthcare professionals. (119, 134, 140, 144)

As part of the cluster-randomised SAFE trial, the impact of screening interventions on patient health status and the acceptability of screening were assessed using baseline, post screening and post study surveys. (118) Self-reported data were collected for anxiety (using the Spielberger 6-item Anxiety Questionnaire), quality of life (using the EuroQol five dimensions (EQ-5D) questionnaire), and surveys also asked about patient views of screening. (119) However, comparisons were not reported for the health status and acceptability of AF detection from patients with AF identified from routine care. (118)

All patients that attended for an ECG in the intervention arms (n=2,595) received a post-screening survey; there were 1,940

(74.8%) participants that responded with a completed survey. Data for anxiety scores were skewed with nearly 40% of all patients reporting the lowest anxiety score. (119) There were no significant differences in the anxiety scores between those that received opportunistic and systematic screening. (119) Hobbs et al. also reported, from other domains in the post screening survey, that 1,810/1,897 (95.4%) of patients felt screening was important and that the minority of patients would have wanted 'someone to discuss it more first' (91/1,892 (4.8%)), 'to talk about the tests with doctor first' (60/1,892 (3.2%)) or 'to come to a clinic appointment for more information' (74/1,892 (4.0%)). Furthermore, only 17/1,897 (3.7%) felt that screening was inconvenient. (119)

Finally, randomly selected participants in the intervention arms that also received baseline questionnaires about anxiety and quality of life were also sent an end of study survey. From 777 surveys distributed, there were 630 (81.1%) responses, of which 535 (68.9%) were completed. There were no significant differences in anxiety scores between the intervention arms at the end of the study. The anxiety and quality of life scores were similar for survey respondents at baseline and at the end of the study, but the authors did not report a direct statistical comparison between the two. (119) Sub-group analyses did however find that the end of

study anxiety scores were significantly higher (mean (95% CI) anxiety score 38.12 (35.89-40.35) versus 34.61 (32.41-36.81); p=0.028) and the quality of life scores were significantly lower (mean (95% CI) EQ-5D score 0.66 (0.62-0.70) versus 0.73 (0.68-0.77); p=0.020) for screen-positive than screen-negative patients. (119) However these findings have limited utility for the effects of screening on the health status of patients, as there were no comparisons made with the health impact of AF detection from routine care.

As part of the SEARCH-AF study pharmacists received training about AF. (134) Knowledge of AF was assessed before training and at end of the study using a survey of eight questions and analysis of ECGs to give a cumulative maximum score of 23 points. The questionnaire ascertained data about general AF knowledge, associated health risks, symptoms, risk factors, stroke risk, screening modes and medications. (134) Lowres et al. reported that the mean (SD) percentage scores for pharmacist knowledge about AF improved from 49% (25) at baseline to 86% (8) post-study (p<0.001). (134) The SEARCH-AF study was also evaluated by a qualitative sub-study; nine pharmacists were interviewed to explore their experiences of implementing an AF screening service. (144) Lowres et al. reported that screening for AF was well accepted in pharmacies and could be linked to the efficient delivery of other healthcare services. (144) Four broad themes were

identified that related to service provision; i) there was interest and engagement in AF screening by pharmacists, customers, and doctors; ii) pharmacists reported perceived benefits from screening that included increased job satisfaction, better customer relations and a raised pharmacy profile; iii) barriers were identified that included managing workflow and allocating time to discuss the screening process and fears; and iv) there was potential for future implementation within this setting with remuneration linked to government or pharmacy incentives by combining AF screening with cardiovascular screening, and automating risk-assessments using touch-screen technology. (144)

The other pharmacy based AF screening study by Walker et al. investigated single-lead ECG screening. (140) All patients that undertook screening (n=121) completed a questionnaire. Patients with screen-detected AF were referred to their usual GP for further management. Walker et al. reported that 'pharmacists and participants found the heart monitor easy to use, and participating GPs had overwhelmingly positive feedback on the study.' (140) However, the authors did not report any methodological or outcome data to support these conclusions. (140)

Although these studies report a positive impact and acceptability of AF screening by patients and pharmacists, there were no studies

that evaluated the views of other healthcare professionals who are more likely to be responsible for delivering AF screening in a primary care setting, such as General Practitioners and nurses. Moreover, there were no studies that investigated the feasibility of implementing screening within primary care settings.

In summary, these studies suggest that AF screening is likely to be acceptable to patients and healthcare professionals, such as pharmacists, but no studies were found that investigated the acceptability of AF screening by GP or nurses. There were no studies that reported comparisons between the impact and/or acceptability of AF screening in those who had AF detected from screening interventions and those with AF identified from routine practice.

2.3. Conclusion and areas for further research

2.3.1. Conclusion

A broad literature review was conducted to provide greater understanding of the research gaps, as previously highlighted by the review by Allaby in 2014 (chapter one), and characterise research priorities before screening implementation.

There have been few randomised trials that have compared the effectiveness of interventions to detect silent AF with AF detection

from routinely delivered primary care. Most evidence for interventions to detect incident AF has been derived from uncontrolled studies of AF case finding. Moreover, there have also been few trials comparing the effectiveness of different screening approaches with one another.

Studies used opportunistic and systematic approaches for screening and the abundance of research investigated AF detection at a single time-point. Within studies of single time-point screening there were two further methods for detecting AF – one-step screening (where patients receive an ECG) or two-step screening (where patients are checked for a pulse irregularity and those with suspected AF receive an ECG). For the vast majority of studies the final AF diagnosis was made using ECGs that were interpreted by cardiac specialists.

The limited evidence does suggest AF screening is likely to be effective at detecting incident AF and comparisons suggest the most cost-effective approach may be opportunistic AF detection. The yield of detecting silent AF appears greater in primary healthcare settings (such as GP practices or out-patient clinics) and in older patients, particularly ≥65 years of age. Patients with screen-detected AF have stroke risk profiles that would warrant treatment with oral anticoagulation. However, there was little data

from one study that reported longer-term clinical outcomes from the treatment of patients with screen-detected AF; this showed no difference in minor adverse effects from the treatment of AF in those with screen-detected AF and those with routinely detected AF. There were no studies that reported outcomes such as the disease progression of AF and changes in stroke burden in those with screen-detected AF. Economic modelling from randomised trial data suggests the most cost-effective approach to screening may be opportunistic screening using the two-stage method AF detection. Furthermore, it appears that AF screening in primary care is acceptable to patients and community pharmacists.

The UK studies of interventions to detect silent AF comprised two randomised trials, one secondary analysis of trial data and four uncontrolled studies of AF case finding. The UK studies investigated single time-point screening in patients ≥65 years of age and involved mostly GPs and/or nurses for undertaking screening activities within GP practices. One of these studies was the SAFE study, the largest randomised trial of AF screening interventions; this found that screening, irrespective of approach used, was both effective and cost-effective at detecting incident AF and secondary analyses suggested that patients with screen-detected had stroke risk scores sufficiently high to warrant anticoagulation treatment.

Moreover, SAFE trial data suggested that screening was acceptable by patients.

2.3.2. Justification for research undertaken within the thesis

Areas for further research that are specific to the work undertaken within this PhD are provided below.

Recommendations currently advocate the two-step approach for AF screening at a single time-point using pulse palpation followed by confirmatory 12-lead ECG.

These recommendations may assume pulse palpation to be the optimal method of detecting pulse irregularities attributable to AF. However, more recently it appears that other methods, such as single-lead ECGs, are increasingly being used for detecting suspected AF. There were no studies that compared the effectiveness of different methods for detecting pulse irregularities as part of the first-step within screening interventions. Indeed, comparing the diagnostic accuracies and effectiveness of different methods for detecting pulse irregularities attributable to AF would help inform our understanding of how this first-step of proposed AF screening could be optimally organised.

The second-step of recommended AF screening is to diagnose AF using 12-lead ECG interpreted by a competent professional - the gold-standard test for AF diagnosis. The majority of studies investigating the detection of silent AF used ECGs interpreted by trained cardiac specialists for the diagnosis of AF. Few studies used other healthcare professionals, such as primary care physicians, for interpreting ECGs when making the final diagnosis of AF. As primary care is a likely setting for AF screening, an important consideration would be to understand the range and accuracies of other methods for interpreting ECGs, such as automated software ECG analysis and primary care physician ECG interpretation. This would enable greater understanding of how AF diagnosis, the second-step of AF screening, could be better organised and implemented within a primary care setting.

Furthermore, it is unclear whether AF screening could be feasibly implemented within primary care. A few studies evaluated the opinions of pharmacists about screening implementation but most screening studies in primary care involved GPs and/or nurses. It is likely that GPs and/or practice nurses would be expected to have a major role in screening activities within primary care. However, there have been no studies evaluating the opinions of these healthcare professionals about feasibly implementing AF screening within General Practice.

Chapter 3. Research aims and objectives

3.1. Aims

The overall aims of this work were to determine how AF screening might feasibly and effectively be introduced into primary care in the UK.

3.2. Objectives

The objectives for this work were:

- To determine the range and accuracies of methods for detecting pulse irregularities attributable to AF.

- To determine the range and accuracies of methods for diagnosing AF using 12-lead ECG.

- To investigate the feasibility and opinions of healthcare professionals in primary care about the implementation of AF screening.

3.3. Research methods

Three complimentary studies were undertaken to investigate each of the three objectives and overall aims:

- A systematic review and meta-analysis of methods for detecting pulse irregularities caused by AF.

- A systematic review and meta-analysis of methods for diagnosing AF using 12-lead ECG.

- A survey of healthcare professionals in primary care about the implementation of AF screening.

Chapter 4. Systematic review and meta-analysis of methods for detecting pulse irregularities caused by atrial fibrillation

4.1. Background

Screening for AF in primary care has been recommended (80, 108, 145) but is yet to be implemented into routine clinical practice. (115) Current recommendations advocate screening to be undertaken as a two-stage process. (80, 108) The first step of this process is to identify patients with a pulse irregularity (i.e. suspected AF) and recommendations advocate using pulse palpation as the method for doing this. (16, 80, 108)

The accuracy of methods for detecting pulse irregularities that are caused by silent AF is particularly important for this first-step of AF screening.

Evaluating the accuracy of diagnostic tests requires knowledge of sensitivity and specificity. (146) Sensitivity and specificity are measures defined according to disease status; the sensitivity of a test is the probability that the index test result will be positive in a person with the disease (or the true positive rate) and the specificity of a test is the probability that the index test result will

be negative in a person without the disease (or the true negative rate). (146)

A high sensitivity would ensure people are appropriately referred for diagnostic 12-lead ECG but a low sensitivity would result in a high false negative rate and mean excessive AF diagnoses are missed. A high specificity is also important and ensures people without AF are correctly identified, but a low specificity would result in a high false positive rate of suspected AF with many patients subsequently having unnecessary ECG examinations.

A systematic review in 2006 by Cook et al. investigated the accuracy of pulse palpation for the detecting AF. (147) Cook et al. identified three studies (n=2,385 patients) that compared the accuracy of pulse palpation with ECG diagnosed AF. (147) Pulse palpation was found to have a pooled sensitivity (95% CI) of 94% (84–97) and pooled specificity (95% CI) of 72% (69–75). (147) Therefore, this review found that despite pulse palpation having a high accuracy for correctly identifying those with AF, this method was less accurate in correctly identifying people without AF resulting in substantial false positive cases of suspected AF. (147)

More recently, new methods for detecting suspected AF have been developed including non-12-lead ECG (e.g. single lead ECG), (126,

133, 140, 148) modified blood pressure monitors (148) and pulse oximeters. (148) To date there has been no systematic evaluation of the range and accuracies of newer methods for detecting pulse irregularities attributable to AF and how these compare to pulse palpation. Indeed, this would inform how the first-step of proposed AF screening could be optimally organised.

4.2. Aims

To describe and compare the diagnostic accuracies of different methods for identifying pulse irregularities caused by AF.

4.3. Objectives

- To describe the healthcare settings and professionals involved the detection of an irregular pulse and potential AF.

- To describe different methods used for detecting pulse irregularities caused by AF.

- To determine the accuracy of different methods used for the detection of an irregular pulse and potential AF as compared to ECG diagnosed AF.

4.4. Methods

4.4.1. Search strategy and selection criteria

This study was conducted in accordance with guidelines and methods for systematic reviews and meta-analyses of diagnostic tests. (146, 149-151) A comprehensive search strategy was used to maximise the sensitivity of literature searching and ensure all relevant citations were identified.

4.4.1.1. Data sources

The databases MEDLINE, EMBASE, Cumulative Index to Nursing & Allied Health (CINAHL) and Latin American and Caribbean Health Sciences Information System (LILACS) were searched in all languages (150) published until 16th March 2015 (Appendix 1). Additionally, the Cochrane Register of Diagnostic Test Accuracy Studies and the reference lists of national guidelines, review articles and included studies were hand-searched to identify potentially eligible studies. (150)

4.4.1.2. Search terms

Studies of diagnostic test accuracy investigate the performance of tests in the context of population, disease state and setting. The search criteria therefore included specified terms to encompass these domains and related to participants, settings, target

condition, index test(s) and reference standard (Appendix 1). (149, 150)

4.4.1.3. Inclusion and exclusion criteria

After the removal of duplicate records, two reviewers (JT and MJ) independently screened citations for relevance and reviewed full-text articles using predetermined eligibility criteria. Any disagreements were resolved by consensus with a third reviewer (TC).

The inclusion criteria for studies in the review were:

- All randomised trials and observational studies

- Studies which recruited participant's ≥18 years of age.

- Studies that involved healthcare professionals identifying patients with an irregular pulse (the participants)

- Studies investigating any method of identifying patients with an irregular pulse or suspected AF (the index test and target condition).

- Studies that compared the index test with any ECG interpreted by a competent professional (the reference standard).

- Studies that reported sufficient data to enable the calculation of diagnostic accuracy.

The exclusion criteria for studies in the review were:

- Studies that were case reports and case-series.

- Studies using invasive or echocardiographic methods of identifying AF, as these could not feasibly be used in population screening.

4.4.2. Data extraction

Two reviewers (JT and MJ) independently extracted data from eligible studies using a pre-specified data extraction form. (Appendix 2) Any disagreements were resolved by consensus with a third reviewer (TC). Data were extracted for study characteristics and for true positive, true negative, false positive and false negative cases of suspected AF.

Where studies reported findings using multiple thresholds for the same intervention, only the data where thresholds maximised the sensitivity of the index test were extracted in order to avoid duplicate inclusion of the same index test. This would have minimised the effects of including duplicate data from the same study within the analyses, which would have inappropriately overinflated the estimates of diagnostic accuracy for an individual test.

The lead author(s) of studies for which the reported data were insufficient to calculate diagnostic accuracy were contacted to ascertain missing data. Studies were excluded from the review if no additional data were identified or if the authors failed to respond.

4.4.3. Assessment of study quality and risk of bias

The assessment of methodological quality and bias is an essential component of systematic reviews as errors in the design, conduct and/or reporting of studies are potential sources of bias. (151) There are three broad types of tools that can be used for the assessment of study quality and bias in systematic reviews – checklists, scales and levels of evidence. (151) Scales provide numerical scores that are attributed to domains based upon perceived importance of the individual domains, but weighting of each item within such scales is often ignored. (152, 153) Consequently, quality-rating scores may not accurately reflect study quality. (152, 153) Levels of evidence amalgamate quality item scores into recommendations and it is therefore not possible to differentiate the individual quality aspects of study. (151) The guidance provided by the Cochrane collaboration for the methodological assessment of study quality within reviews of diagnostic test accuracy advocate using checklists, as this enables

full reporting of study characteristics without assumptions being made or emphasis being placed on individual quality items. (151)

A systematic review by Whiting e al. identified over 90 instruments that have previously been used to assess study quality in reviews of diagnostic test accuracy. (154) This review found that there were large variations in the items used within the tools for assessing study quality and that most tools were developed for specific use within an individual review. Furthermore, none of the tools have been systematically evaluated. (151, 154)

Therefore, study quality in the current review was appraised using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) instrument. (151, 155-157) The QUADAS-2 tool was first developed through expert consensus, informed by empirical evidence, (155, 157) and is recommended by the Cochrane Collaboration for assessing the risk of bias in systematic reviews of diagnostic test accuracy. It was recently updated to ensure it remained fit for purpose. (155) The QUADAS-2 tool currently rates study quality across two broad areas – the 'risk of bias' within the study methods and 'applicability' of the research question to the study methods. Within these two areas of assessment, there are four domains that are evaluated - patient selection, the index test, the reference standard, study flow and timing. To make a

judgment about these four domains there are a number of 'signalling questions' that enable each domain to be judged by consensus from question responses. (155)

The QUADAS-2 does not explicitly evaluate studies investigating multiple tests. When studies in the current review investigated multiple index tests, the QUADAS-2 tool was applied separately for each test to ensure the risk of bias was assessed for every test being evaluated.

One of the limitations of the QUADAS-2 tool is that is does not enable grading and sub-group analyses according to study quality. To enable sub-group analyses according the study quality, the studies included in the review were also graded using a four-point quality scale that has been derived from the QUADAS-2 criteria and has been previously reported by Van den Bruel et al. (158) Studies were rated as grade A if they fulfilled all QUADAS-2 criteria. Studies were graded D if there was no or unclear verification of the index test findings with the reference standard, or if the index test results were interpreted un-blinded to the results of the reference test. Studies where there was an unduly long time delay between index and reference tests, or where the reference test was not independent of the index test, or where the reference test was interpreted un-blinded to the results of the index test were graded

C. Remaining studies which did not fall in to these categories were graded B. (158)

4.4.4. Statistical analysis

Analyses were conducted using Stata Version 11.0 and Review Manager 5.2 for quality assessments.

4.4.4.1. Primary outcome measures for diagnostic accuracy

Data extracted were used to construct 2x2 contingency tables and primary outcomes were the pooled sensitivity, specificity, Positive likelihood ratios (PLR) and negative likelihood ratios (NLR) of each method for detecting suspected AF. (146)

Unlike sensitivity and specificity, likelihood ratios make explicit the impact of the test result on the probability of disease and therefore provide a more obvious expression of test performance. (159) A PLR describes how many times more likely the positive index test results are in the diseased group than the non-diseased group. Conversely, a NLR describes how many times less likely the negative index test results are in those with the disease than those without disease. (146) As a guide, a PLR over 10 suggests a useful increase in probability of disease after a positive test result and a NLR of less than 0.1 is a useful decrease in probability of disease after a negative test result. (160)

Sensitivity and specificity are inherently related, and vary by the threshold used for diagnostic tests and heterogeneity between studies. (146, 161) Univariate meta-analysis of these measures is therefore inappropriate, as it does not take into account the correlation between these measures and results in an underestimation of test accuracy. (161) The most rigorous approach for deriving point estimates of sensitivity, specificity, PLR and NLR requires fitting of random effects hierarchical models of meta-analysis. (146)

A number of statistical models are available for conducting meta-analyses of diagnostic test accuracy. The Moses Littenberg model, although the oldest and widely used, is a fixed effects model and does not take into account the heterogeneity between studies. (146) This has been superseded by random effects models of meta-analysis. Consequently, the bivariate hierarchical method was used for the primary analyses as this provides greater precision of point estimates for diagnostic accuracy. (146, 162) This model involves statistical distributions at two levels. At a lower level, the cell counts in the 2×2 tables are extracted from each study using binomial distributions and logistic (log-odds) transformations of proportions. At a higher level, random study effects are assumed to account for heterogeneity in diagnostic test accuracy between

studies beyond that accounted for by sampling variability at the lower level. (146) The bivariate parameterization models sensitivity, specificity and the correlation directly between them. The inclusion of a correlation parameter in the model allows for the expected trade off in sensitivity and specificity as the test positivity threshold varies across studies. Where variation between studies arises through such a trade off this correlation is expected to be negative, but the correlation may be positive if there are other sources of heterogeneity. (146)

Using this statistical method, the average operating points (pooled estimates) for sensitivity and specificity were calculated and this enabled the construction of Summary Receiver Operating Characteristic (SROC) plots with 95% prediction regions. (146)

SROC plots provide a visual display of the results from individual studies in Receiver Operating Characteristic (ROC) space; each study is plotted within the SROC plot as a single sensitivity 1-specificity point and the size of the point represents the sample size of the study. (146) Therefore, SROC plots provide a visual scatter of study results. A diamond within the SROC plots represents the pooled sensitivity and specificity, and a 95% prediction region can also be calculated and displayed which can be used as a method of visually assessing heterogeneity. (146, 163) A

greater test accuracy is observed when the pooled sensitivity-specificity plot is closer to top left hand corner within the SROC plot.

4.4.4.2. Assessment of heterogeneity

Heterogeneity is presumed in meta-analyses of diagnostic test studies as this will arise from differences in study design, patient characteristics, test methods and other unknown factors. (146, 164) To minimise heterogeneity the results were analysed a priori in groups of each method for identifying an irregular pulse.

Univariate tests of heterogeneity in sensitivity and specificity, such as the I^2 statistic, cannot be reliably used for the assessment of heterogeneity in reviews of diagnostic test accuracy. (165) Alternatively, it is recommended that heterogeneity can be assessed by visual inspection of the SROC plot 95% prediction regions and how close individual studies were to the predicted ROC curve within SROC plots. (146, 163, 164)

4.4.4.3. Sub-group analyses

Sub-group analyses were planned according to study quality and studies conducted within a primary care setting providing there were ≥4 studies within sub-groups. (146) The bivariate hierarchical model assumes the inclusion of at least four studies and sub-

groups with fewer studies results in failure of the hierarchical model to converge and greater statistical error. (146)

4.4.4.4. Assessment of publication bias

The assessment of publication bias using conventional funnel plot asymmetry, as for systematic reviews of interventions, is not recommended; application of these methods to reviews of diagnostic test accuracy may lead to inaccuracy and increase the risk of inappropriately detecting publication bias. (166) It is well established that the accuracy of conventional tests for assessing funnel plot asymmetry is reasonable if odds ratios are close to one (as in the case for many randomised trials), but this deteriorates as the odds ratios move away from one. (146, 166) For diagnostic test accuracy reviews the odds ratios are expected to be large. Applying conventional tests for funnel plot asymmetry in diagnostic test accuracy reviews is therefore likely to result in publication bias being incorrectly indicated more often. (146, 166) Consequently, a more appropriate method of assessing publication bias has been developed. (146, 166) Deeks' funnel plot asymmetry tests for the association between the diagnostic accuracy and the 'effective sample size', a simple function of the number of diseased and non-diseased individuals. This test has been shown to have a moderate power for detecting funnel plot asymmetry. (146, 166) Therefore, an assessment for publication bias was made within each category

of method for detecting suspected AF using Deeks' Funnel plot asymmetry test; a P-value<0.10 was used to signify the presence of publication bias. (166)

4.5. Results

After the removal of duplicate records, there were 5,418 potential citations identified. From these, 69 studies were identified for detailed evaluation (figure 4-1). After full-text review, 21 studies were included in the final analyses (Table 4-1). (119, 120, 126, 134, 167-183) Five studies met the selection criteria, but reported insufficient outcome data and were excluded (Table 4-2). (137, 184-187)

Figure 4-1: Study selection and stratification

| CINAHL 638 citations | EMBASE 3344 citations | LILACS 61 citations | MEDLINE 3194 citations | Reference List 4 citations | Contact with authors 1 citation |

7242 titles or abstracts identified and screened for retrieval

7173 excluded:
- 1824 duplicate records
- 5349 not relevant

69 full-text articles

48 excluded:
- 31 not detection studies
- 3 editorials or reviews
- 9 not relevant to study design
- 5 insufficient data

21 studies included in final review

Table 4-1: Characteristics of included studies

Study	Setting, population & sample size	Prevalence/ proportion (%) of AF	Study Design†	Index test(s)	Reference test	Outcomes	Quality grading
Bourdillon 1978 (167)	UK; secondary care; 221 ECGs of adult subjects	18.6	CS	Software interpretation of three lead ECG	12-lead ECG interpreted by two clinicians	Sensitivity 0.66, specificity 0.99	C
Caldwell 2012 (168)	UK; secondary care; 157 patients recruited from anticoagulation clinic	49.7	CC	1. Five second conventional 6-lead ECG from 4 limb leads 2. Five second 6-lead frontal plane ECG from four electrodes in a supine, undressed patient using a prototype recorder 3. Five second 6-lead frontal plane ECG using four electrodes in a sitting, dressed patient using a prototype recorder Cardiologist interpretation (all tests)	12-lead ECG interpreted by three cardiologists	Test 1: sensitivity 0.96; specificity 0.97 Test 2: sensitivity 0.96; specificity 0.97 Test 3: sensitivity 0.95; specificity 0.97	B
Doliwa	Sweden;	51	CC	Bipolar single-lead	12-lead ECG	Sensitivity 0.92;	D

2009 (126)	secondary care; 100 patients recruited from cardiology outpatient clinic			ECG placed on the patient's thumbs Cardiologist interpretation	interpreted by a cardiologist	specificity 0.96	
Gregg 2008 (169)	UK; secondary care; database of 50,000 hospital ECGs; 1,785 randomly selected	6.1	CS	1. Reconstructed 12-lead ECG from limb leads and leads v1 and v4. 2. Reconstructed 12-lead ECG from limb leads and leads v2 and v5 All index tests interpreted by computer software	12-lead ECG interpreted by two cardiologists	<u>Test 1:</u> sensitivity 0.84; specificity 0.99 <u>Test 2:</u> sensitivity 0.88; specificity 0.99	D
Haberman 2015 (170)	USA; secondary care; 381 subjects recruited from university athletics society, medical students, and cardiology clinic	4.7	CS	iPhone based single lead ECG (AliveCor) interpreted by software and two electrophysiologists	12-lead ECG interpreted by automated software and two electrophysiologists	Sensitivity 0.94; specificity 0.99	D
Hobbs 2005 (119)	UK; primary care; 9,866 patients aged≥ 65 years	<u>Test 1:</u> 8.6 <u>Test 2:</u> 8.5 <u>Test 3:</u> 8.2	RCT	1. Pulse palpation (nurse) 2. Single-lead ECG (nurse interpretation)	12-lead ECG interpreted by two cardiologists; third cardiologist for arbitration	<u>Test 1:</u> sensitivity 0.87; specificity 0.81 <u>Test 2:</u> sensitivity 0.69; specificity	C

		Test 4: 9.1 Test 5: 9.4		3. Single-lead ECG (GP interpretation) 4. Limb-lead ECG (nurse interpretation) 5. Limb-lead ECG (GP interpretation)		0.83 Test 3: sensitivity 0.85; specificity 0.86 Test 4: sensitivity 0.72; specificity 0.83 Test 5: sensitivity 0.83; specificity 0.89	
Kaleschke 2009 (171)	Germany; secondary care; 508 patients attending AF specialist centres	25.4	C	Single-lead ECG Omron Heartscan 801) Cardiologist interpretation	12-lead ECG interpreted by a cardiologist.	Sensitivity 0.99; specificity 0.96	B
Kearley 2014 (172)	UK, primary care; 999 patients aged ≥75 years	Test 1: 7.7 Test 2: 7.9 Test 3: 7.9 Test 4: 7.9 Test 5: 7.9	CS	1. Pulse palpation (nurse) 2. Automated BP monitor (WatchBP) 3. Single-lead ECG with automated analysis (OMRON HCG-801) 4. Single-lead ECG with cardiologist interpretation	12-lead ECG interpreted by two cardiologists; third cardiologist for arbitration	Test 1: sensitivity 0.97; specificity 0.86 Test 2: sensitivity 0.95; specificity 0.90 Test 3: sensitivity 0.99; specificity 0.76 Test 4: sensitivity 0.94, specificity	B

				(OMRON HCG-801)		0.95	
				5.Single-lead ECG with cardiologist interpretation (Merlin)		Test 5: sensitivity 0.94, specificity 0.90	
Lau 2012 (173)	Australia; 109 patients; setting unknown	35.8	CC	Single-lead ECG using smart phone (i-phone) ECGS interpreted by automated software and cardiologist	12-lead ECG interpreted by a cardiologist	Software interpretation: sensitivity 1; specificity 0.96 Cardiologist interpretation: sensitivity 0.97; specificity 0.91	B
Lowres 2015 (134)	Australia; primary care; 972 patients recruited from 10 pharmacies	6.9	CS	Pulse palpation conducted by trained pharmacist	iPhone based single lead ECG (AliveCor heart monitor) interpreted by cardiologist	Sensitivity 0.76; specificity 0.93	D
Marazzi 2012 (174)	Italy; Secondary care; 550 patients attending hypertension clinic	20.1 20.4	CS	1. Automated BP monitor (Microlife BP A200 Plus) 2. Automated BP monitor (Omron M6)	12-lead ECG interpreted by a cardiologist.	Microlife BP A200 Plus: sensitivity 0.92; specificity 0.97 Omron M6: sensitivity 1; specificity 0.96	B
McManus 2013 (175)	USA; Secondary care; 76 patients with AF attending elective	50	CS	The index test was the Smart phone application to detect fingertip pulse waveform i-	12-lead ECG or telemetry, interpreted by a trained physician	RMSSD: sensitivity 0.98; specificity 0.91 Shannon entropy:	D

107

	cardioversion			phone 4S) Analysis by three methods of automated software (RMSSD, Shannon entropy and combination of the two)		sensitivity 0.98; specificity 0.82 RMSSD + Shannon entropy: Sensitivity of 0.96; specificity 0.95.	
Morgan 2002 (120)	UK; Primary care; 3001 patients from four general practices	6.1	RCT	Pulse palpation (nurse)	Single-lead ECG interpreted by a physician	Sensitivity 0.91; specificity 0.74	A
Renier 2012 (176)	Belgium; secondary care; 244 patients attending emergency department or hospital wards	7.3	CS	Non-12 –lead (Omron Heartscan - a wireless device which creates a ECG on a display representing leads v3 and v4 of a conventional 12-lead ECG) Interpretation by two GPs and automated software	12-lead ECG interpreted by a cardiologist.	GP interpretation: sensitivity 0.69; specificity 0.95 Software interpretation: sensitivity 0.92; specificity of 1	B
Somerville 2000 (177)	UK; Primary care; 86 patients recruited from one general practice	Pulse palpation: 31.4 Bipolar ECG:	CC	1. Pulse palpation (nurse) 2. Bipolar ECG (nurse	12-lead ECG interpreted by a consultant cardiologist	Test 1: sensitivity 0.97; specificity 0.79 Test 2: Sensitivity	C

		30.2		interpretation) 3. Bipolar ECG (GP interpretation)		0.94; specificity 0.93 Test 3: Sensitivity 0.96; specificity 0.98	
Stergiou 2009 (178)	Greece; Secondary care; 73 patients recruited from both outpatient and inpatient settings	36.9	CC	Automated BP monitor (Microlife BPA100 Plus)	12-lead ECG interpreted by the lead investigator and a cardiologist	Sensitivity 1; specificity 0.85	D
Sudlow 1998 (179)	UK; primary care; 1235 patients from nine general practices.	4.4	CC	Pulse palpation (nurse)	Limb-lead ECG (interpreter unclear)	Sensitivity 0.93; specificity 0.71 in women, and 1 and 0.86 in men respectively	D
Vaes 2014 (180)	Belgium; primary care; 181 patients from general practices	53	CC	Single lead ECG (MyDiagnostick) with automated software analysis	12-lead ECG interpreted by cardiologist	Sensitivity 0.94; specificity 0.93	B
Wiesel 2004 (181)	USA; secondary care; 450 patients recruited from outpatient clinic	12.6	CS	Automated BP monitor (Omron 712C)	12-lead ECG (interpreter unclear)	Sensitivity 1; specificity 0.91	D
Wiesel 2009 (182)	USA; secondary care; 405 patients recruited from outpatient clinic	23.0	CS	Automated BP monitor (Microlife BP3MQ1-2D)	12-lead ECG interpreted by a cardiologist	Sensitivity 0.95; specificity 0.86	B
Wiesel	USA; secondary	5.7	C	Automated BP	ECG event monitor	Sensitivity 1;	B

| 2013 (183) | care; 160 patients ≥65 years recruited from internist's office and home monitoring performed. | | | monitor (Microlife BP3MQ1-2D) | (Heartrak 2)

A 60 second ECG interpreted by a cardiologist | specificity 0.94 | |

†CC = Case-control study; CS = cross-sectional study; RCT = Randomised controlled Trial; C = Cohort study

Table 4-2: Characteristics of eligible studies that were excluded

Author/Year	Setting, population & sample size	Study design	Intervention	Comparator	Reported outcomes	Reason for exclusion
Boyle 2013 (184)	USA; 1334 patients; screening performed at community events	CS	Pulse palpation (Nurse)	Single lead ECG rhythm strip interpreted by consultant cardiologist	Pulse palpation: Sensitivity 0.43; Positive predictive value 0.16	Only the number of true AF cases were reported
Harrington 2013 (185)	USA; 93 patients; setting unknown	C	Smart phone application (i-Phone 4S with three algorithms)	Smart phone application (i-Phone 4S with three interpretation algorithms): Algorithm 1: Poincare Plot+RMSSD+ ShE Algorithm 2: Poincare Plot+RMSSD+ SampE Algorithm 3: Poincare Plot+RMSSD+ ShE+SampE	Algorithm 1: Sensitivity 1; specificity 0.88 Algorithm 2: Sensitivity 1; specificity 0.87 Algorithm 3: sensitivity 1; specificity 0.98	Unsure of comparator intervention, and true positive cases of AF not known
Lewis 2011 (186)	UK and USA; secondary care; 594 patients ≥60 years recruited	CC	Finger probe that recorded pulse waveform (automated	12-lead ECG interpreted by a consultant cardiologist	Sensitivity 1; specificity 0.91	The number of true positive and true negative cases not

	outpatient clinics		software analysis)			reported
Rhys 2013 (137)	UK; primary care; patients ≥65 years recruited from flu clinics	CS	Pulse palpation (Nurse)	12-lead ECG interpreted by a consultant cardiologist	23 patients were detected as having AF	Only true positive cases of AF reported
Sawant 2014 (187)	USA; secondary care; 103 patients from cardiology outpatient clinic	CS	Smartphone ECG interpreted by cardiologist	12-lead ECG interpreted by two cardiologists	Sensitivity 0.88; specificity 0.91	Number of patients with true AF not reported

†CC = Case-control study; CS = cross-sectional study; RCT = Randomised controlled Trial; C = Cohort study

4.5.1. Study characteristics

Of the 21 studies included, (table 4-1) there were two randomised-trials, (119, 120) seven case-control, (126, 168, 173, 177-180) two cohort, (171, 183) and 10 cross-sectional studies. (134, 167, 169, 170, 172, 174-176, 181, 182)

Although the majority of studies avoided a case-controlled design, only four were prospective and there were seven studies conducted in a primary care setting.(119, 120, 134, 172, 177, 179, 180) AF prevalence ranged from 5.7% to 25.4% in studies with a prospective design. (119, 120, 171, 183) There was substantial variation in the proportion and/or prevalence of AF in studies within each category of detection method.

Five studies excluded participants if they were <65 years of age and for two studies the age of inclusion was 75 years. (119, 134, 172, 177-179, 183) Six studies included participants who were ≥18 years old. (120, 171, 174-176, 181) Nine studies excluded patients that had been fitted with pacemakers and/or implantable defibrillators. (134, 169, 172, 174, 178, 180-183)

4.5.2. Healthcare settings for detecting pulse irregularities caused by atrial fibrillation

Of the 21 included studies eight were conducted in the UK (119, 120, 167-169, 172, 177, 179) and six in non-UK European countries. (126, 171, 174, 176, 178, 180) Five studies were conducted in the United States (170, 175, 181-183) and two in Australia. (134, 173)

Most studies were conducted in secondary care settings (126, 167-171, 174-176, 178, 181-183) with only seven being conducted in primary care. (119, 120, 134, 172, 177, 179, 180) Five of these were in UK primary care. (119, 120, 172, 177, 179) The healthcare setting for one study was not reported. (173)

4.5.3. Methods used to detect pulse irregularities caused by atrial fibrillation

4.5.3.1. Detecting pulse irregularities and suspected atrial fibrillation

The 21 studies investigated 39 interventions (n=15,129 pulse assessments) which were categorised as blood pressure monitors (BPMs) [six studies; seven interventions], (172, 174, 178, 181-183) non-12-lead ECG [10 studies; 20 interventions], (119, 126, 167-169, 171, 172, 176, 177, 180) pulse palpation [six studies; six interventions], (119, 120, 134, 172, 177, 179) and smartphone

applications [three studies; six interventions]. (170, 173, 175) The five studies which were excluded due to insufficient reporting of outcome data investigated pulse palpation, pulse oximetry, smart phone applications and single-lead ECG as methods for detecting AF.

Of the studies investigating BPMs, three did not report the professional used to obtain readings, (174, 178, 181) one study used a nurse, (172) one used a trained technician (182) and another used patient self-recording of automated blood pressures. All of the studies of BPMs (172, 174, 178, 181-183) used integrated automated analysis within the BPM to determine the presence of suspected AF. (183) Most of these studies described the software algorithms used; blood pressure monitors analysed the differences in time between successive pulse waveforms during blood pressure cuff deflation and suspected AF was indicated when a pre-specified irregularity index was exceeded. (174, 178, 181-183)

Of the studies that investigated smart phone devices for detecting an irregular pulse, two required patients to self-administer the device to detect AF (170, 175) and for one study the method used to obtain a reading was not reported. (173) All of the studies of smart phone technology used software algorithms, as for BPMs, to

detect pulse irregularities caused by AF. (170, 173, 175) One study however combined software and electrophysiologist analysis of the readings to determine suspected AF. (170)

There was a broader range of approaches for indicating the presence of suspected AF in studies that used non-12-lead ECGs. (119, 126, 167-169, 171, 172, 176, 177, 180) To obtain the non-12-lead ECGs there were two studies where patient's self- recorded ECGs. (126, 171) Nurses recorded ECGs in three studies (119, 172, 177) but for the remainder of studies the person recording ECGs was not reported. (167-169, 176, 180) Seven of the non-12-lead ECG studies used clinical expertise of clinicians to interpret ECGs – four studies used cardiologists (126, 168, 171, 172) and three studies used GPs and/or nurses. (119, 176, 177) Only one study reported a one-hour training session that was provided to clinicians to standardise ECG interpretation. (119) However, none of the studies provided information about the criteria used to rule in or out the presence of suspected AF and this classification threshold was based on clinical expertise.

The remaining studies used automated software analysis of non-12-lead ECGs but the algorithms and the cut-offs used to determine the presence of suspected AF were not reported. (167, 169, 172, 180)

In studies that used pulse palpation for detecting pulse irregularities caused by AF (119, 120, 134, 172, 177, 179) most used nurses to perform pulses palpation (119, 120, 172, 177, 179) and one used community pharmacists. (134) All studies relied on the clinical expertise of healthcare professionals to make judgments about the degrees of pulse irregularity when determining the presence of suspected AF. Two studies classified the pulse as either regular or irregular, the latter being used to determine the presence of AF. (119, 177) One study defined suspected AF as being any pulse that was not regular. (179) One study required nurses to palpate the pulse for at least 20 seconds and then classify the pulse as either regular, occasional ectopics, frequent ectopics or continuously irregular; suspected AF was then defined as any pulse irregularity. (120) Two studies did not report how pulses were classified to determine suspected AF. (134, 172) Only one study reported training provided to nurses about detecting an abnormal pulse. (119)

4.5.3.2. Reference standard for atrial fibrillation detection

For the majority of studies, the reference standard was 12-lead ECG interpreted by at least one trained physician/cardiologist. One study did not specify the training of the clinician interpreting reference ECGs. (167) Five studies reported other reference standards; (120, 134, 175, 179, 183) one study used either 12-

lead ECG or ECGs derived from cardiac telemetry; (175) three studies used single or limb-lead ECG; (120, 134, 179) one study used ECGs derived from Holter monitors. (183)

4.5.4. Study quality and risk of bias

The methodological quality of included studies using QUADAS-2 criteria is presented in figure 4-2. Study quality was generally low. Using the additional quality grading system, we classified one study as A-grade having met all QUADAS-2 criteria. (120) Eleven studies were graded category C or D. (119, 126, 134, 167, 169, 170, 175, 177-179, 181) Studies with the lowest methodological quality (D-grade) were classified as this due to either the interpretation of the reference standard being unclear or at high risk of bias, or due to the index test being interpreted un-blinded to the results of the reference standard. Category C studies were graded as such because it was unclear whether there was an appropriate time interval between the index test and reference standard. The remaining nine studies were categorised as grade-B in methodological quality. (168, 171-174, 176, 180, 182, 183)

Figure 4-2: Study quality according to QUADAS-2 criteria

Figure 4-2: Study quality according to QUADAS-2 criteria

4.5.5. Data synthesis

Forest plots for diagnostic accuracies of the four methods for detecting AF are presented in figures 4-3, 4-4, 4-5 and 4-6. Blood pressure monitors (BPMs) had a pooled sensitivity of 0.98 (95% CI 0.92-1) and specificity of 0.92 (95% CI 0.88-0.95); PLR of 12.1 (95% C.I 8.2-17.8) and NLR of 0.02 (95% C.I 0.00-0.09). There were similar diagnostic accuracies for studies that investigated smartphone applications, sensitivity 0.97 (95% CI 0.95-0.99), specificity 0.95 (95% CI 0.88-0.98), PLR 19 (95% C.I 8-45), NLR 0.03 (95% C.I 0.01-0.05); and non-12-lead ECGs, sensitivity 0.91 (95% CI 0.86-0.94), specificity 0.95 (95% CI 0.92-0.97), PLR 20.1 (95% C.I 12-33.7), NLR 0.09 (95% C.I 0.06 to 0.14). Although pulse palpation had a sensitivity that was comparable to the other methods for detecting suspected AF (sensitivity of 0.92 (95% CI 0.85-0.96), there was a substantially lower specificity for this method (specificity 0.82 (0.76-0.88); PLR and NLRs for pulse palpation were 5.2 (95% C.I 3.8-7.2) and 0.1 (0.05-0.18), respectively.

Figure 4-3: Sensitivity and specificity of blood pressure monitor interventions

AUTHOR YEAR	SENSITIVITY (95% CI)	AUTHOR YEAR	SPECIFICITY (95% CI)
Kearley 2014	0.95 [0.88 – 0.99]	Kearley 2014	0.90 [0.88 – 0.92]
Marazzi 2012	0.92 [0.85 – 0.97]	Marazzi 2012	0.97 [0.95 – 0.99]
Marazzi 2012	1.00 [0.96 – 1.00]	Marazzi 2012	0.94 [0.92 – 0.96]
Sterigou 2009	1.00 [0.95 – 1.00]	Sterigou 2009	0.85 [0.78 – 0.91]
Wiesel 2004	1.00 [0.94 – 1.00]	Wiesel 2004	0.91 [0.87 – 0.93]
Wiesel 2009	0.95 [0.92 – 0.97]	Wiesel 2009	0.86 [0.84 – 0.89]
Wiesel 2013	1.00 [0.63 – 1.00]	Wiesel 2013	0.94 [0.88 – 0.97]
COMBINED	0.98 [0.92 – 1.00]	COMBINED	0.92 [0.88 – 0.95]

Figure 4-4: Sensitivity and specificity of non-12-lead ECG interventions

AUTHOR YEAR	SENSITIVITY (95% CI)	AUTHOR YEAR	SPECIFICITY (95% CI)
Bourdillon 1978	0.66 [0.49 – 0.80]	Bourdillon 1978	0.99 [0.96 – 1.00]
Caldwell 2012	0.95 [0.87 – 0.99]	Caldwell 2012	0.97 [0.91 – 1.00]
Caldwell 2012	0.96 [0.89 – 0.99]	Caldwell 2012	0.97 [0.91 – 1.00]
Caldwell 2012	0.96 [0.89 – 0.99]	Caldwell 2012	0.97 [0.91 – 1.00]
Doliwa 2009	0.92 [0.81 – 0.98]	Doliwa 2009	0.96 [0.86 – 1.00]
Gregg 2008	0.88 [0.80 – 0.93]	Gregg 2008	0.99 [0.98 – 0.99]
Gregg 2008	0.84 [0.76 – 0.91]	Gregg 2008	0.99 [0.98 – 0.99]
Hobbs 2005	0.69 [0.60 – 0.76]	Hobbs 2005	0.83 [0.81 – 0.85]
Hobbs 2005	0.85 [0.78 – 0.90]	Hobbs 2005	0.86 [0.84 – 0.88]
Hobbs 2005	0.72 [0.63 – 0.80]	Hobbs 2005	0.83 [0.81 – 0.85]
Hobbs 2005	0.83 [0.75 – 0.89]	Hobbs 2005	0.89 [0.87 – 0.90]
Kaleschke 2009	0.99 [0.96 – 1.00]	Kaleschke 2009	0.96 [0.94 – 0.98]
Kearley 2014	0.94 [0.85 – 0.98]	Kearley 2014	0.90 [0.88 – 0.92]
Kearley 2014	0.95 [0.88 – 0.99]	Kearley 2014	0.95 [0.93 – 0.96]
Kearley 2014	0.99 [0.93 – 1.00]	Kearley 2014	0.76 [0.73 – 0.79]
Renier 2012	0.92 [0.64 – 1.00]	Renier 2012	1.00 [0.98 – 1.00]
Renier 2012	0.69 [0.39 – 0.91]	Renier 2012	0.95 [0.90 – 0.97]
Somerville 2000	0.96 [0.80 – 1.00]	Somerville 2000	0.98 [0.91 – 1.00]
Somerville 2000	0.94 [0.84 – 0.99]	Somerville 2000	0.93 [0.86 – 0.97]
Vaes 2014	0.94 [0.87 – 0.98]	Vaes 2014	0.93 [0.85 – 0.97]
COMBINED	0.91 [0.86 – 0.94]	COMBINED	0.95 [0.92 – 0.97]

Figure 4-5: Sensitivity and specificity of smartphone applications
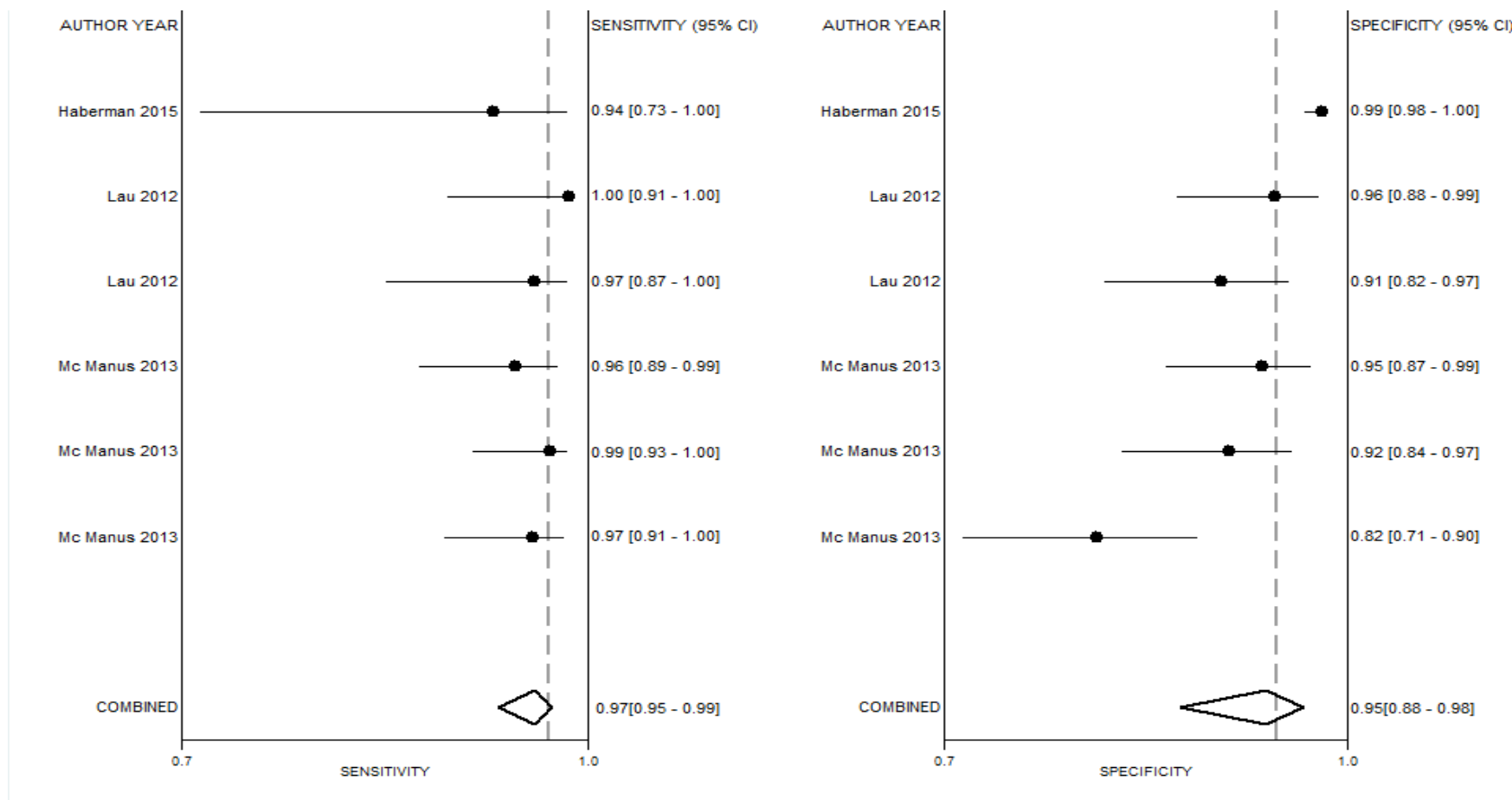
Figure 4-6: Sensitivity and specificity of pulse palpation
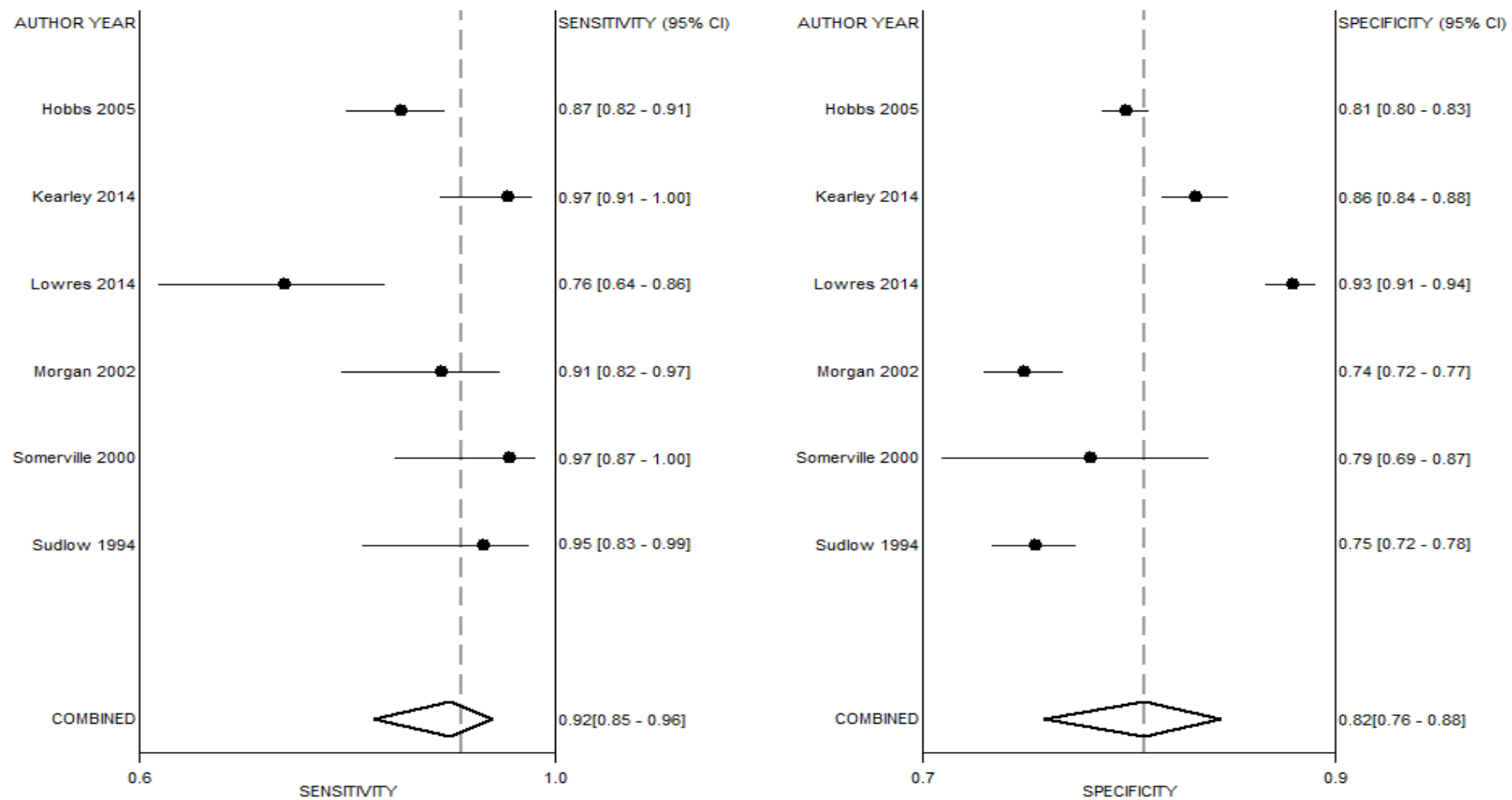
SROC plots for the methods of detecting AF are presented in figure 4-7. Visual inspection of the plots confirms the accuracy of pulse palpation was lower than other methods for detecting AF. There was substantial variation in outcomes of the studies investigating non-12-lead ECG from the predicted ROC curve and suggests the heterogeneity amongst these studies was greatest. In contrast, the heterogeneity was lowest amongst studies that investigated smart phone applications and BPMs for detecting pulse irregularities caused by AF.

Figure 4-7: Summary Receiver Operating Characteristic (SROC) plots for methods of detecting pulse irregularities caused by atrial fibrillation
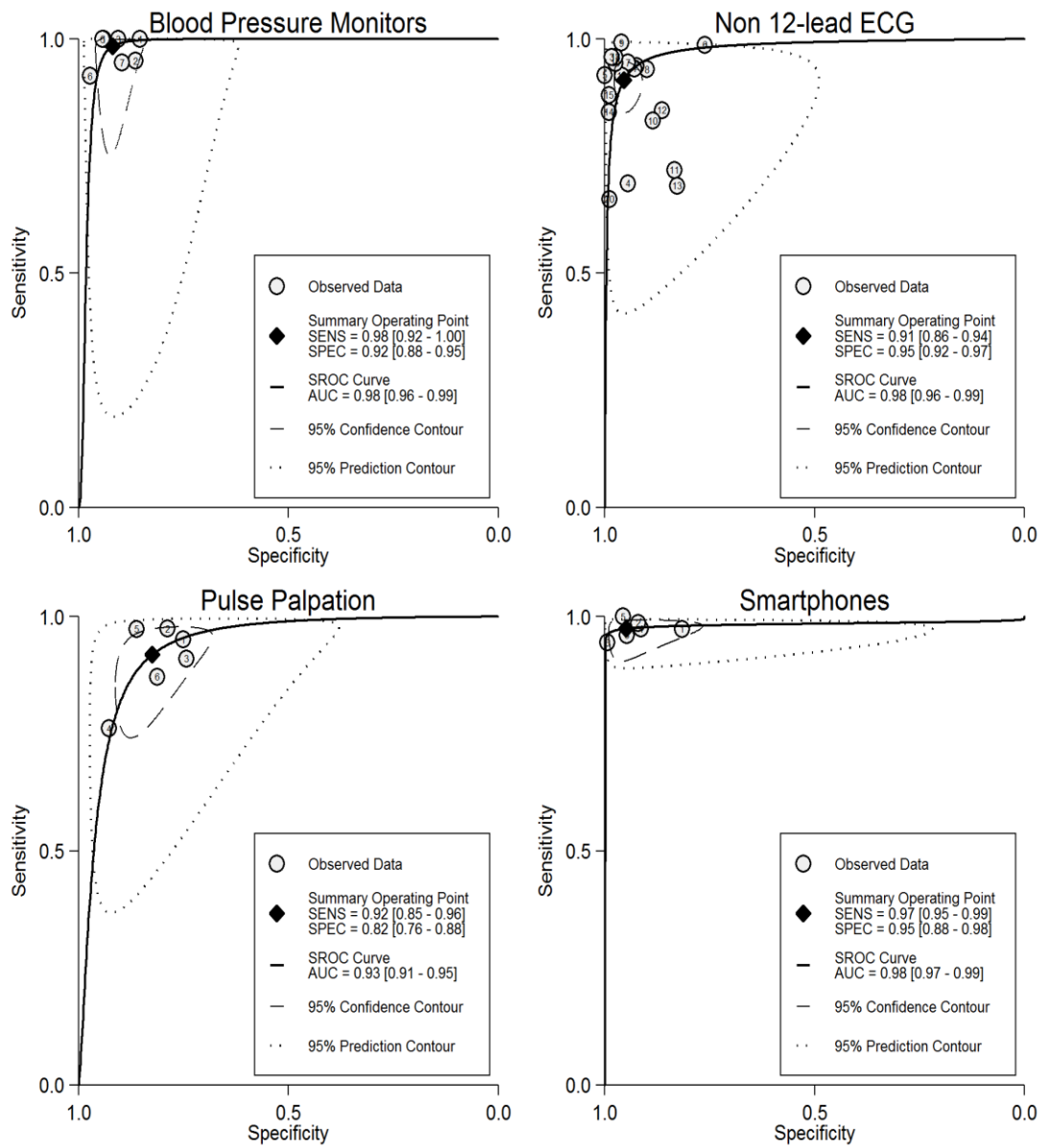
4.5.6. Sub-group analyses

There were only sufficient studies to perform bivariate sub-group analyses according to study quality for BPM, non-12-lead ECG and pulse palpation interventions. After exclusion of studies with the lowest (D-grade) quality, there were no substantial differences to the primary findings. [BPMs: sensitivity 0.96 (95% C.I 0.91-0.98), specificity 0.93 (95% C.I 0.89-0.96); non-12-lead ECG: sensitivity 0.92 (95% C.I 0.86-0.95), specificity 0.94 (95% C.I 0.91-0.97); pulse palpation: sensitivity 0.93 (95% C.I 0.86-0.97), specificity 0.81 (95% C.I 0.76-0.85)].

Sufficient studies to perform bivariate sub-group analyses for primary care studies were available for pulse palpation and non-12-lead ECG interventions. The findings were similar to our primary analyses, although the specificity of non-12-lead ECGs was slightly lower [Non-12-lead ECGs: sensitivity 0.91 (95% C.I 0.83-0.95), specificity 0.89 (95% C.I 0.85-0.92); pulse palpation: all studies were conducted in primary care and findings already presented above].

4.5.7. Publication bias

There was no evidence of publication bias; Deeks' Funnel test p=0.34, p=0.11, p=0.14 and p=0.27 for studies investigating

BPMs, non-12-lead ECG, smart phone applications and pulse palpation, respectively.

4.6. Discussion

4.6.1. Summary of principal findings

Modified blood pressure monitors (BPMs), non-12-lead ECGs, smart phone applications and pulse palpation were identified as methods for detecting pulse irregularities caused by AF. Most studies investigating these methods were conducted in secondary care settings although most primary care studies were from the UK. Healthcare professionals were often involved in the detection of suspected AF. Automated analysis was used by BPMs and smart phone applications to detect cases of suspected AF, but for pulse palpation and non-12-lead ECGs the presence or absence of possible AF was often determined by clinician expertise. Modified BPMs and non-12-lead ECG devices were found to have the greatest diagnostic accuracy for detecting pulse irregularities caused by AF. Although the sensitivities of all methods for identifying those with suspected AF were similar, the specificity of pulse palpation was lower which gives rise to more false positive test results.

4.6.2. Strengths and limitations

This study supersedes the previous review by Cooke et al. (147) that provided evidence for the accuracy of pulse palpation for detecting suspected AF. The current study is also the first systematic review and meta-analysis of different interventions for

the detection of suspected AF and provides evidence comparing the diagnostic accuracy of newer interventions to pulse palpation.

A strength of this study was the use of a standardised protocol that is consistent with published guidelines for systematic reviews of diagnostic test studies. A comprehensive search strategy was used that included contacting authors of potentially relevant studies, although no additional data were obtained from author correspondence.   The results also supported the lack of publication bias and it is likely that relevant small studies with less significant findings were included.

There were four studies that were excluded due to insufficient reporting of outcome data to enable meta-analysis and this could influence the findings. However, the outcomes that were reported from these studies were consistent with the primary outcomes from the review and the effect of excluding these studies is likely to be minimal.

Only four of the 21 included studies adopted a prospective design and there were a number of inherent methodological weaknesses in most studies as reflected by the assessments of study quality. Only one study was judged to have met all QUADAS-2 criteria. Consequently, the internal validity of the findings may be limited.

Most studies that investigated methods for identifying patients with an irregular pulse were conducted in a secondary care setting and there was substantial variation in the proportion of patients with AF. Combined with the abundance of low quality of studies in the review, the generalisability of the findings to primary care populations that AF screening is intended for is limited. Healthcare professionals in secondary care may have greater training and experience for detecting patients with AF – either using pulse palpation or newer technologies - than those in primary care, and patients in secondary care are more likely to have cardiovascular disease and AF detected than unselected primary care populations. Consequently this limits the translation of findings from the review to screening conducted within primary care settings.

As the prevalence of AF increases with age and it is greater in men than women, it is possible that the performance of methods for detecting pulse irregularities could be affected by the different ages and distribution of gender between study populations. A limitation of this study was that these potential interacting factors could not be accounted for as the included studies did not provide sufficient data for such analyses to be conducted. However, the measures of diagnostic accuracy used in the review are prevalence independent and therefore the impact of age within studies on test performance is likely to be mitigated.

For some studies the time between conduct of index and reference tests was unclear. Patients with paroxysmal AF could have been missed as AF identified by initial testing may have resolved by the time verification testing had been performed. Consequently, this could have reduced the diagnostic accuracy of the index test(s) under investigation.

As expected, there was heterogeneity amongst the studies within all intervention categories and this is likely to be attributable to differences in study population and design. This variation was greatest for studies that investigated non-12-lead ECG for detecting suspected AF. This may be due to differences in the detection methods within this category; the non-12-lead ECG interventions included single-lead, three-lead and reconstructed ECG for detecting pulse irregularities caused by AF, and such technological differences may account for some of the greater observed heterogeneity than other methods. In addition, there would have been differences in the abilities of clinicians, such as GPs or nurses, to verify the presence or absence of disease in these studies and the criteria used to interpret non-12-lead ECGs to rule in or out suspected AF were often undefined and reliant upon clinical expertise.

4.6.3. Findings in context of previous research

A narrative literature review was conducted to inform the Royal College of Physicians about how to best detect AF. This review also identified, in addition to pulse palpation and single-lead ECGs, modified blood pressure monitors and pulse oximeters as methods for detecting pulse irregularities caused by AF. (148) Harris et al. suggested that pulse palpation may have the lowest accuracy for detecting an irregular pulse caused by AF than other methods due to its lower specificity and these findings are consistent with those in my review. However, the review by Harris et al. only included studies from 2006 onwards, did not provide point estimates for the diagnostic accuracies or compare the accuracies of different methods for detecting suspected AF, and the risk of bias of included studies were not appraised. (148) Therefore, the internal validity of findings from this earlier review are limited and the findings from my review supersede it.

The systematic review by Cooke et al. only investigated the accuracy of pulse palpation for detecting AF. (147) My review identified a greater number of studies that investigated pulse palpation for detecting AF and investigated other methods of detecting pulse irregularities. The findings from my review are consistent with those by Cooke et al. and support the assertion

that pulse palpation, despite having a high sensitivity, has a low specificity for the detection of pulse irregularities caused by AF.

More recently, studies have tended to evaluate newer technologies for detecting suspected AF. My review identified three methods – non-12-lead ECG, modified blood pressure monitors, smart phone applications – as alternative methods for detecting an irregular pulse caused by AF. Of all interventions analysed, pulse palpation was found to have the lowest diagnostic accuracy for detecting pulse irregularities attributable to AF as reflected by its lower specificity. This could be due to differences between the cut-off points of each method to rule in or out the presence of suspected AF. Electronic methods, such as modified blood pressure monitors or smart phone applications, use software algorithms to determine the severity of pulse irregularity and only those patients meeting a pre-determined cut-off point are classified as having AF. In contrast, studies investigating pulse palpation required clinicians to classify the pulse as being regular or irregular. It is therefore conceivable that pulse palpation is more likely to result in a greater number of false positive cases of suspected AF arising from the detection of patients who have a slight irregularity in pulse that is not attributable to AF, such as atrial or ventricular extra-systoles, that software algorithms would have excluded.

4.7. Conclusion

Modified blood pressure monitors and non-12-lead ECG devices were found to have a greater accuracy than pulse palpation for detecting pulse irregularities attributable to AF. These methods could be pragmatic alternatives to the currently recommended pulse palpation for identifying patients with suspected AF as part of national screening programmes.

This study investigated and compared the accuracies of different methods that could be used for the first-step of proposed AF screening. In the next chapter, I will investigate and compare the accuracies of different methods that could be used to interpret 12-lead ECGs – the proposed second-step of AF screening.

Chapter 5. Systematic review and meta-analysis of methods for diagnosing atrial fibrillation using 12-lead ECG

5.1. Background

After firstly identifying patients with a pulse irregularity (i.e. suspected AF), the second-step of recommended AF screening is to confirm or exclude the presence of AF. (80, 108) The gold standard test for diagnosing AF is 12-lead ECG that is interpreted by a competent professional. (51, 80, 108)

The accuracy of interpreting 12-lead ECGs for the diagnosis of AF is fundamental to the effectiveness of AF screening, and has significant implications for health service resources and patient safety. A high sensitivity would result in patients being correctly diagnosed with AF and appropriately assessed for stroke preventative therapies, but a low sensitivity would result in excessive false negative diagnoses of AF and patients incorrectly being reassured and not offered treatment. Conversely, a high specificity would result in those without AF being correctly reassured, but a low specificity would result in high numbers of false positive AF diagnoses and patients inappropriately offered stroke preventative treatment.

A sub-study of the systematic screening versus routine practice for the detection of atrial fibrillation in people aged 65 and over (SAFE) trial investigated the accuracy of different methods for 12-lead ECG interpretation and diagnosis of AF. (188) The SAFE sub-study compared the accuracy of ECG interpretation by GPs, practice nurses and automated software to cardiologist ECG interpretation. (188) This found that, compared to ECG diagnoses of AF made by cardiologists, interpretive software had a significantly greater specificity than the other methods of ECG interpretation. However, the sensitivities for GPs, nurses and software for AF diagnosis were substantially lower and similar across all groups. [Sensitivities (95% CI) and specificities (95% CI) for GPs: 79.8% (70.5-87.2) and 91.6% (90.1-93.1); practice nurses: 77.1% (67.4-85.0) and 85.1% (83.0-86.9); automated software: 83.3% (78.3-88.2) and 99.1% (98.7-99.5)]. Consequently, Mant et al. suggested the accuracy of ECG interpretation and diagnosis of AF in primary care using any single method may be insufficient for screening implementation within this setting. (188)

To date there has been no systematic evaluation of the accuracies of different methods for interpreting 12-lead ECGs in the diagnosis of AF. A greater understanding of this fundamental step of AF screening, with a focus of AF diagnosis in primary care, would

inform how the second-step of screening could be organised and implemented.

5.2. Aims

To describe and compare the diagnostic accuracies of different methods for 12-lead ECG interpretation in the diagnosis of AF, with a focus on ECG interpretation in primary care.

5.3. Objectives

- To describe the healthcare settings and professionals involved in the interpretation of 12-lead ECGs for AF diagnosis.

- To describe different methods used for interpreting 12-lead ECGs in the diagnosis of AF.

- To determine the accuracy of different methods used for making diagnoses of AF, with a focus on healthcare professionals in primary care, by comparing the interpretation of 12-lead ECGs by trained cardiac specialists to other methods of 12-lead ECG interpretation.

5.4. Methods

The methods used for this systematic review were the same as those in the previous systematic review of interventions for detecting pulse irregularities attributable to AF. Justification for the methodological and statistical approaches used has therefore been provided in the relevant sub-sections of chapter four.

5.4.1. Search strategy and selection criteria

This study was conducted in accordance with guidelines and methods for systematic reviews and meta-analyses of diagnostic tests. (146, 150, 151, 164) A comprehensive search strategy was used to ensure all relevant citations were identified.

5.4.1.1. Data sources

The databases MEDLINE, EMBASE, Cumulative Index to Nursing & Allied Health (CINAHL) and Latin American and Caribbean Health Sciences Information System (LILACS) were searched in all languages published from inception until 24th March 2014 (Appendix 3). (150) Additionally, the Cochrane Register of Diagnostic Test Accuracy Studies and the reference lists of national guidelines, review articles and included studies were hand-searched to identify potential studies. (150)

5.4.1.2. Search terms

The search criteria included specified terms to encompass domains related to the participants, settings, target condition, index test(s) and reference standard (Appendix 3). (149, 150)

5.4.1.3. Inclusion and exclusion criteria

After the removal of duplicate records, two reviewers (JT and MJ) independently screened citations for relevance and reviewed full-text articles using predetermined eligibility criteria. Any disagreements were resolved by consensus with a third reviewer (TC).

The inclusion criteria for studies in the review were:

- All randomised trials and observational studies.

- Studies that recruited participant's ≥18 years of age.

- Studies that investigated any method for interpreting 12-lead ECGs to show AF (the index test and target condition.)

- Studies that compared the index test to 12-lead ECG diagnoses of AF made by a trained cardiac specialist (the reference standard).

- Studies that involved healthcare professionals in making AF diagnoses.

- Studies that reported sufficient data available to enable the calculation of diagnostic accuracy.

The exclusion criteria for studies in the review were:

- Studies that were case reports or case-series.

- Studies using invasive or echocardiographic methods for diagnosing AF, as these could not feasibly be used in population screening.

5.4.2. Data extraction

Two reviewers (JT and MJ) independently extracted data from eligible studies using a pre-specified data extraction form (Appendix 2). Any disagreements were resolved by consensus with a third reviewer (TC). Data were extracted for study characteristics and for true positive, true negative, false positive and false negative diagnoses of AF. The lead author(s) of studies for which reported data were insufficient to calculate diagnostic accuracy were contacted to ascertain missing data.

5.4.3. Assessment of study quality and risk of bias

Study quality was appraised using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) instrument. (151, 155-157) Additionally, the studies were graded using the quality scale reported by Van den Bruel et al; (158) studies were rated as grade A if they fulfilled all QUADAS-2 criteria. Studies were graded D if there was no or unclear verification of the index test findings with the reference standard, or if the index test results were interpreted

un-blinded to the results of the reference test. Studies where there was an unduly long time delay between index and reference test, or where the reference test was not independent of the index test, or where the reference test was interpreted un-blinded to the results of the index test were graded C. Remaining studies which did not fall in to these categories were graded B.

5.4.4. Statistical analysis

Analyses were conducted using Stata Version 11.0 and Review Manager 5.2 for quality assessments.

5.4.4.1. Primary outcome measures for diagnostic accuracy

Data extracted were used to construct 2x2 contingency tables. This enabled the calculation of sensitivity and specificity for each method of diagnosing AF. Positive likelihood ratios (PLR) and negative likelihood ratios (NLR) were calculated for each method of diagnosing AF. Unlike sensitivity and specificity, likelihood ratios make explicit the impact of a positive or negative test result on the probability of/absence of disease and therefore are a more obvious expression of test performance. (152) As a guide, a PLR over 10 suggests a useful increase in probability of disease after a positive test result and a NLR of less than 0.1 is a useful decrease in probability of disease after a negative test result. (153)

Primary outcomes were the pooled sensitivity, specificity, PLR and NLR for each method of diagnosing AF using 12-lead ECG. The bivariate hierarchical random effects method was used to determine the average operating points for sensitivity, specificity, PLRs and NLRs which enabled construction of Summary Receiver Operating Characteristic (SROC) plots with 95% prediction regions. (146) Diagnostic accuracy was assessed by comparison of average operating points and respective 95% confidence intervals.

5.4.4.2. Assessment of heterogeneity

Heterogeneity is presumed in meta-analyses of diagnostic test studies and the I^2 statistic cannot be reliably used for its assessment. (146) Heterogeneity was therefore described by the variation in the outcomes from included studies and our pooled estimates by visual inspection of the SROC plots and how close individual studies lie to the predicted ROC curve. To minimise heterogeneity the results were analysed a priori grouped according to method of diagnosing AF.

5.4.4.3. Sub-group analyses

Sub-group analyses were planned according to study quality and groups of healthcare professionals within a primary care setting. It was expected that sub-groups would be small; therefore univariate random effects meta-analysis was used to derive pooled estimates

for sensitivity and specificity when there were less than four studies within sub-groups as the bivariate model is unreliable in this context. (146)

5.4.4.4. Assessment of publication bias

An assessment of publication bias was made according to categories of method for detecting AF using Deeks' Funnel plot asymmetry test; a P-value<0.10 was used to signify the presence of publication bias. (146, 166)

5.5. Results

After the removal of duplicate records there were 4,426 potential citations, of which 62 were identified as relevant for detailed evaluation (figure 5-1).   After full-text review, 10 studies were included in the final analyses (table 5-1). (119, 137, 167, 169, 177, 189-193) There was one study that met selection criteria for which there were insufficient data for reported outcomes (table 5-2). (194)

Figure 5-1: Study selection and stratification
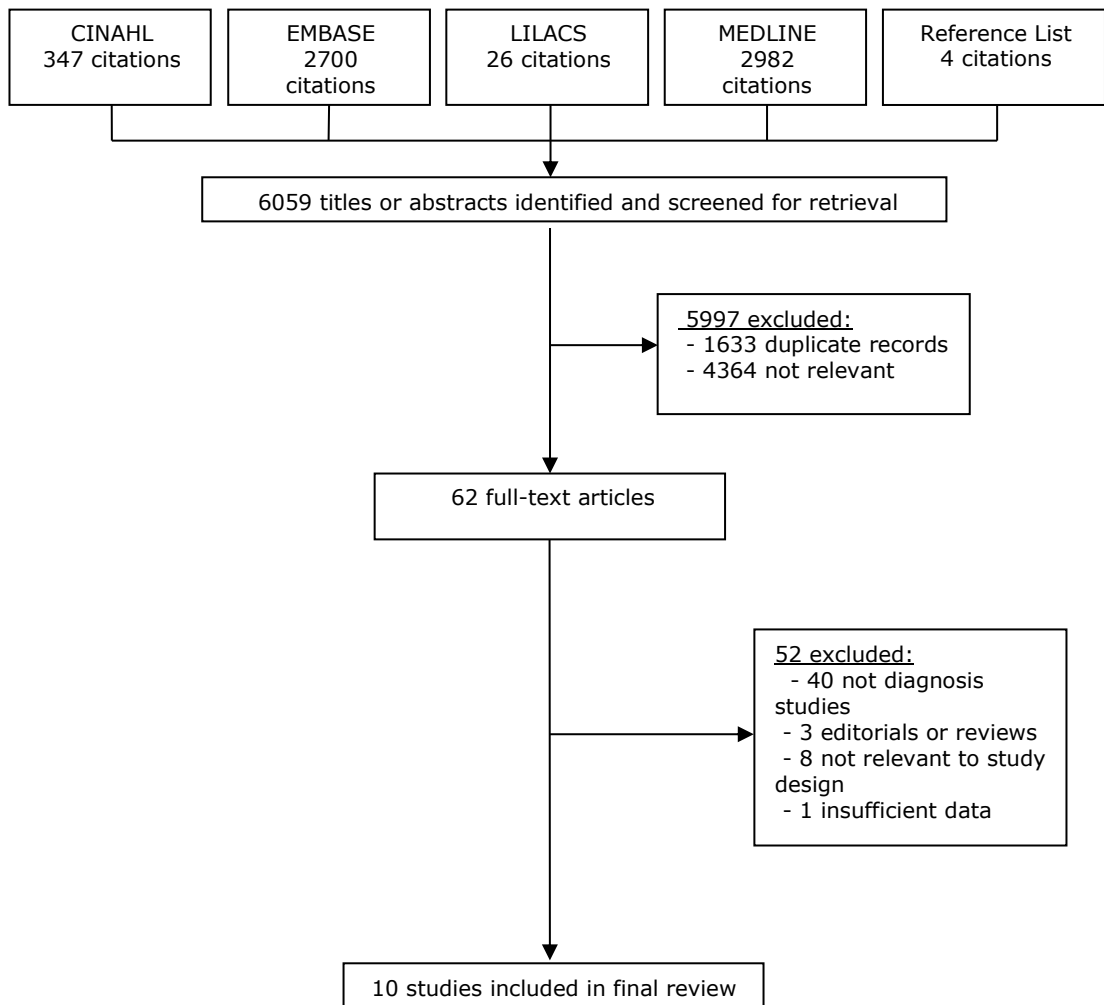
5.5.1. Study characteristics

Of the 10 studies included in the review (table 5-1), there was one randomised trial, (119) two case-control (177, 193) and seven cross-sectional studies. (137, 167, 169, 189-192) Excluding case control designs, across studies the prevalence of AF ranged from 6.7% to 18.6% (Table 5-1).

5.5.2. Healthcare settings for 12-lead ECG interpretation and diagnosis of atrial fibrillation

There were five studies conducted in the UK, (119, 137, 167, 169, 177) three in the USA, (189, 191, 192) one in Europe, (190) and one in Israel. (193) Three studies were conducted in a primary care setting (119, 137, 177) and included participants over 65 years of age; patients were recruited that would have been eligible for AF screening if it were implemented. (119, 137, 177) However, the remainder of studies were conducted using patients with existing cardiac pathologies in secondary care.

5.5.3. Methods used for 12-lead ECG interpretation and diagnosis of atrial fibrillation

5.5.3.1. Methods used for acquiring and interpreting 12-lead ECGs in the diagnosis of atrial fibrillation

The 10 studies investigated a total of 16 methods of diagnosing AF (a total of 55,376 participant ECGs), which were categorised into

two intervention groups: 1) automated software (eight studies; nine diagnostic methods) (119, 137, 167, 169, 189-192) and, 2) any healthcare professional (five studies; seven diagnostic methods). (119, 137, 177, 190, 193) Sub-groups of healthcare professional were defined as: secondary care physicians (two studies; two diagnostic methods) (190, 193) and primary care professionals (three studies; five diagnostic methods), (119, 137, 177) the latter comprising GPs (three studies) (119, 137, 177) and practice nurses (two studies). (119, 177)

Of the included studies, four reported nurses or nurse assistants as the healthcare professionals who performed and acquired ECGs from patients. (119, 137, 177, 190) For the remainder of studies the professionals used to obtain ECGs was not reported.

With the exception of one study, (191) all studies that investigated automated software analysis of ECGs reported the software used to diagnose AF. Both studies that investigated secondary care physician ECG interpretation (190, 193) relied on the clinical experience of the professionals involved to diagnose AF, and one of these studies reported each secondary care physician to have over 30 years of expertise. (190) All studies that investigated ECG interpretation by primary care professionals relied on their clinical experience; (119, 137, 177) one of these studies involved training

being providing to healthcare professionals to improve ECG interpretation prior to study initiation. (119)

5.5.3.2. Reference standard for diagnosing atrial fibrillation

For five studies, the reference standard was 12-lead ECG interpreted by at least two cardiologists. (119, 169, 189, 190, 193) Of the remaining studies, four used ECG interpretation by a single cardiologist as the reference standard and one study used two trained secondary care clinicians. (167)

Table 5-1: Characteristics of included studies

Study	Setting, population & sample size	AF Prevalence/ proportion (%)	Study Design†	Index test(s)	Reference test	Outcomes	Quality grading
Bourdillon 1978 (167)	UK; secondary care; 221 ECGs of adult subjects	18.6	CS	Software interpretation (Mount Sinai)	2 clinicians, independent interpretation	Sensitivity 0.85; specificity 0.98	C
Davidenko 2007 (189)	USA; secondary care; 35,508 consecutive ECGs were reviewed	7.9	CS	Software interpretation (Marquettes)	Interpretation by several cardiologists with a group consensus	Sensitivity 0.97; specificity 1.00	D
Gregg 2008 (169)	UK; secondary care; database of 50,000 hospital ECGs; 1,785 randomly selected	6.1	CS	Software interpretation (Philips)	Interpreted by 2 cardiologists	Sensitivity 0.89; specificity 0.99	D
Hakacova 2012 (190)	Sweden; secondary care; total of 576 ECGs from 503 participants with a mean age of 64 years	10.4	CS	Test 1: Non expert secondary care clinician Test 2: Software A (Philips) Test 3: Software B (Philips)	Interpreted by 2 expert cardiologists	Test 1: Sensitivity 0.86; specificity 0.99 Test 2: Sensitivity 0.92; specificity 0.99 Test 3: Sensitivity 0.68; specificity 0.98	B
Hobbs 2005 (119)	UK; primary care; 9,866 patients aged≥ 65 years, 2595 ECGs were reviewed	6.8 6.7 8.4	RCT	Test 1: General practitioner interpretation Test 2: Practice nurse interpretation Test 3: Software	Interpreted by 2 consultant cardiologists independently, with a third if arbitration was needed	Test 1: Sensitivity 0.80; specificity 0.92 Test 2: Sensitivity 0.77; specificity 0.85 Test 3: Sensitivity 0.83; specificity 0.99	B

					interpretation (Biolog)		
Poon 2005 (191)	USA; secondary care; 4,297 consecutive ECGs were reviewed	6.3	CS	Software interpretation (not specified)	Cardiologist interpretation	Sensitivity 0.91; specificity 0.99	D
Reddy 1998 (192)	USA; secondary care; 10,352 ECGs were reviewed	8	CS	Software interpretation (Mac-rhythm)	Cardiologist interpretation	Sensitivity 0.88; specificity 0.99	D
Rhys 2013 (137)	UK; primary care; patients ≥65 years recruited from flu clinics; 32 ECGs reviewed	6.3	CS	Test 1: Software interpretation (Cardioview) Test 2: General practitioner interpretation	ECG interpreted by cardiologist	Test 1: Sensitivity 1; specificity 1 Test 2: Sensitivity 1; specificity 1	D
Shiyovich 2010 (193)	Israel; secondary care; 268 patient's ECGs	81.7	CC	Secondary care clinician interpretation	Interpretation by 2 senior cardiologists	Sensitivity 0.97; specificity 0.31	B
Somerville 2000 (177)	UK; Primary care; 86 patients recruited from one general practice, 86 ECGs reviewed	31.5 30.2	CC	Test 1: Practice nurse interpretation Test 2: General practitioner interpretation	Interpreted by consultant cardiologist	Test 1: Sensitivity 0.97; specificity 0.88 Test 2: Sensitivity 1; specificity 0.98	B

†CC = Case-control study; CS = Cross-sectional study; RCT = Randomised controlled Trial; C = Cohort study

Table 5-2: Characteristics of eligible studies that were excluded

Author/Year	Setting, population & sample size	Study design	Intervention	Comparator	Reported outcomes	Reason for exclusion
Bogun 2004 (194)	USA; secondary care; database of 2298 ECGs from 1085 patients	Cross sectional	Software interpretation using GE Marqutte 12 SE or MACR programs, overread by cardiologists	Interpretation by 2 electrophysiologists	442 (19%) of the 2298 ECGs had an incorrect computer interpretation of AF in 382 (35%) of patients	Number of true AF, false AF, missed AF, and non AF were not reported

5.5.4. Study quality and risk of bias

Figure 5-2 shows the methodological quality of included studies according to QUADAS-2 criteria was generally low. There were no studies graded as having the highest (A-grade) methodological quality. Five studies with the lowest methodological quality (D-grade) were due to the methodological interpretation of the reference standard being unclear or at high risk of bias. One study was graded as category C because it was unclear whether the reference standard was interpreted without knowledge of the index test.

Figure 5-2: Study quality according to QUADAS-2 criteria

5.5.5. Data synthesis

Automated software was found to have a pooled sensitivity of 0.89 (95% CI 0.82-0.93) and specificity of 0.99 (95% CI 0.99-0.99) for diagnosing AF using 12-lead ECG. (Figure 5-3) This corresponded with a PLR of 96.6 (95% C.I 64.2-145.6) and NLR of 0.11 (95% C.I 0.07-0.18). In contrast, the pooled specificity for the accuracy of any healthcare professional diagnosing AF (Figure 5-4) was lower than automated software although there was a similar sensitivity of this method for interpreting ECGs; sensitivity 0.92 (95% CI 0.81-0.97), specificity 0.93 (95% CI 0.76-0.98), PLR 13.9 (95% C.I 3.5-55.3), NLR 0.09 (95% C.I 0.03-0.22). Figure 5-5 shows the sensitivity and specificity for diagnosing AF by any primary care professionals was similar to any healthcare professionals [sensitivity 0.96 (95% CI 0.66-1.00), specificity 0.94 (95% CI 0.85-0.98), PLR 15.4 (95% C.I 5.9-40.3), NLR 0.05 (95% C.I 0.00 to 0.49)].

Visual inspection of the SROC plots (figure 5-6) confirms there was substantial variation in the outcomes from studies investigating the accuracy of clinicians' 12-lead ECG diagnosis and suggests heterogeneity amongst these studies was greater than the automated software studies.

Figure 5-3: Sensitivity and specificity of 12-lead ECG interpretation using automated software
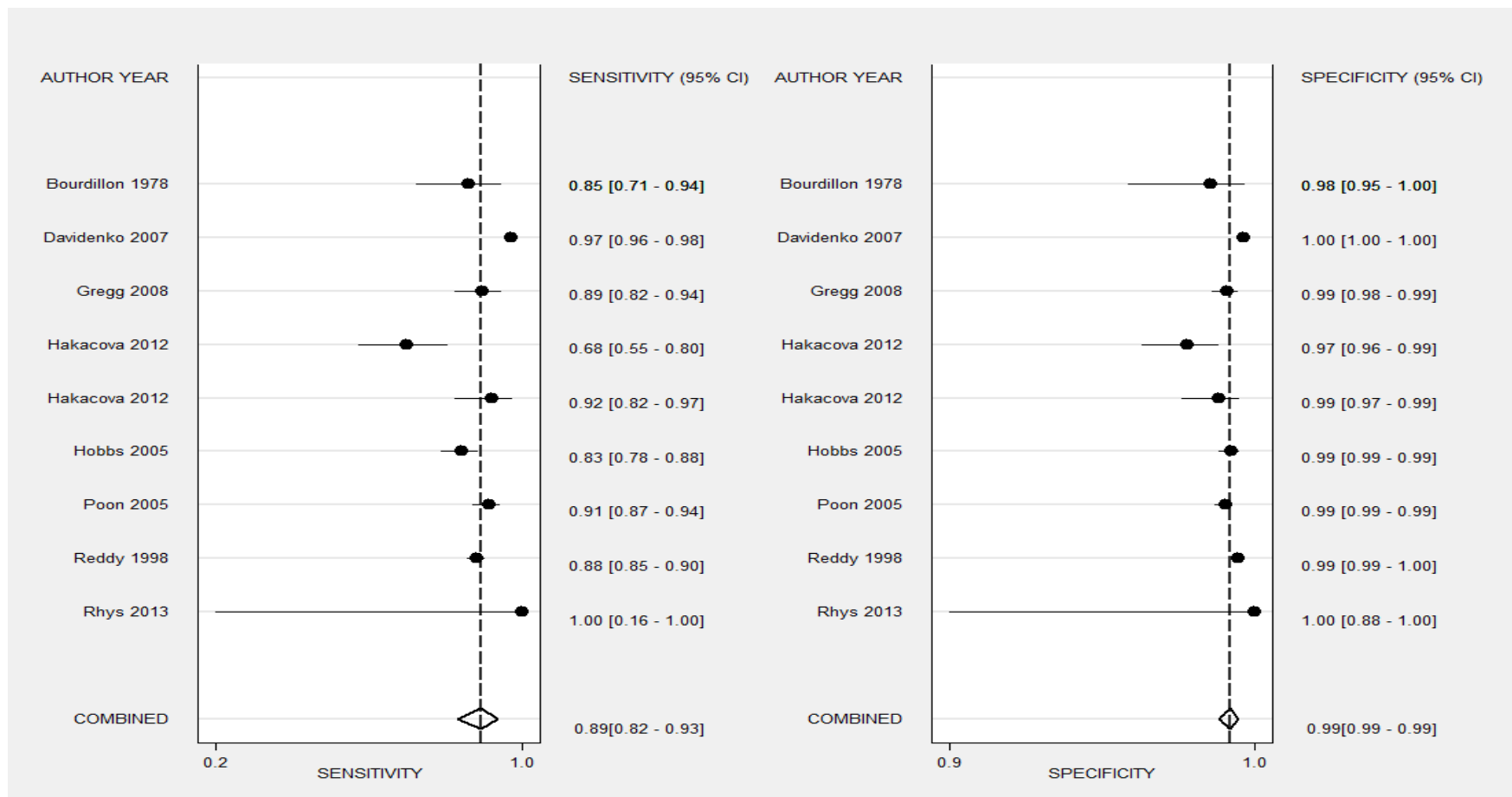
Figure 5-4: Sensitivity and specificity of 12-lead ECG interpretation by any healthcare professional
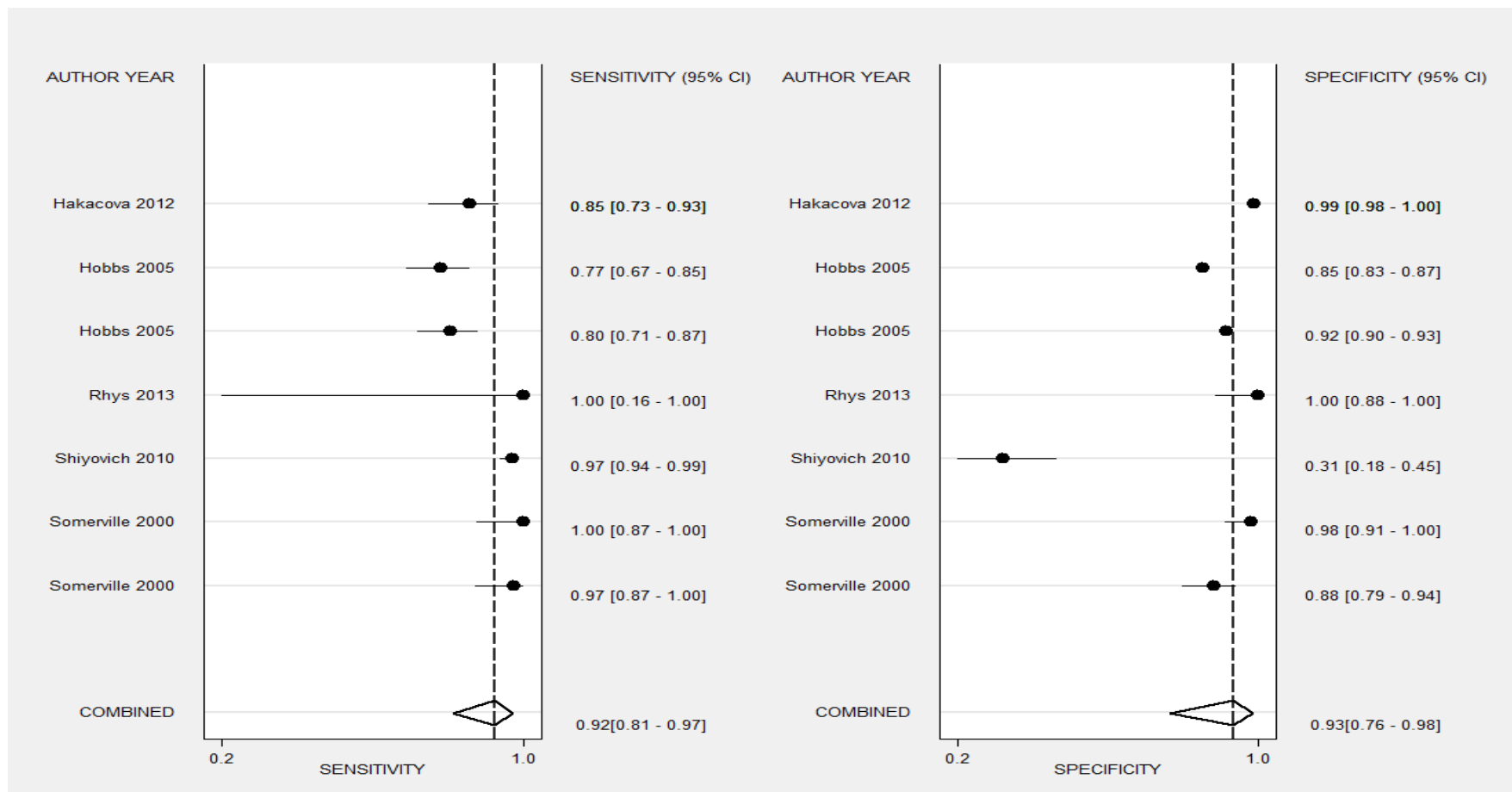
Figure 5-5: Sensitivity and specificity of 12-lead ECG interpretation by primary care professionals
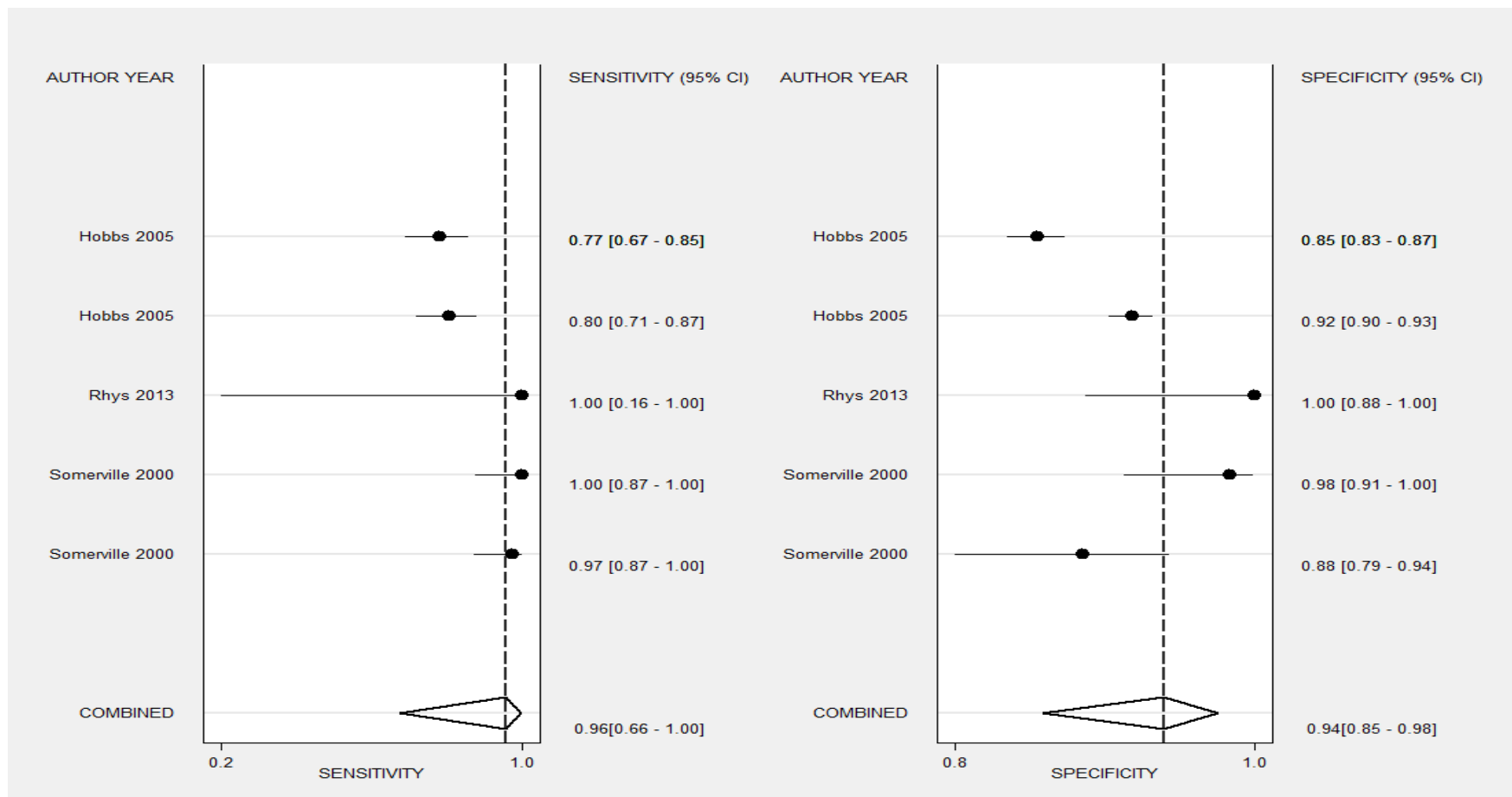
Figure 5-6: Summary Receiver Operating Characteristic (SROC) plots for the accuracy of 12-lead ECG interpretation by software, any clinician, and primary care clinician
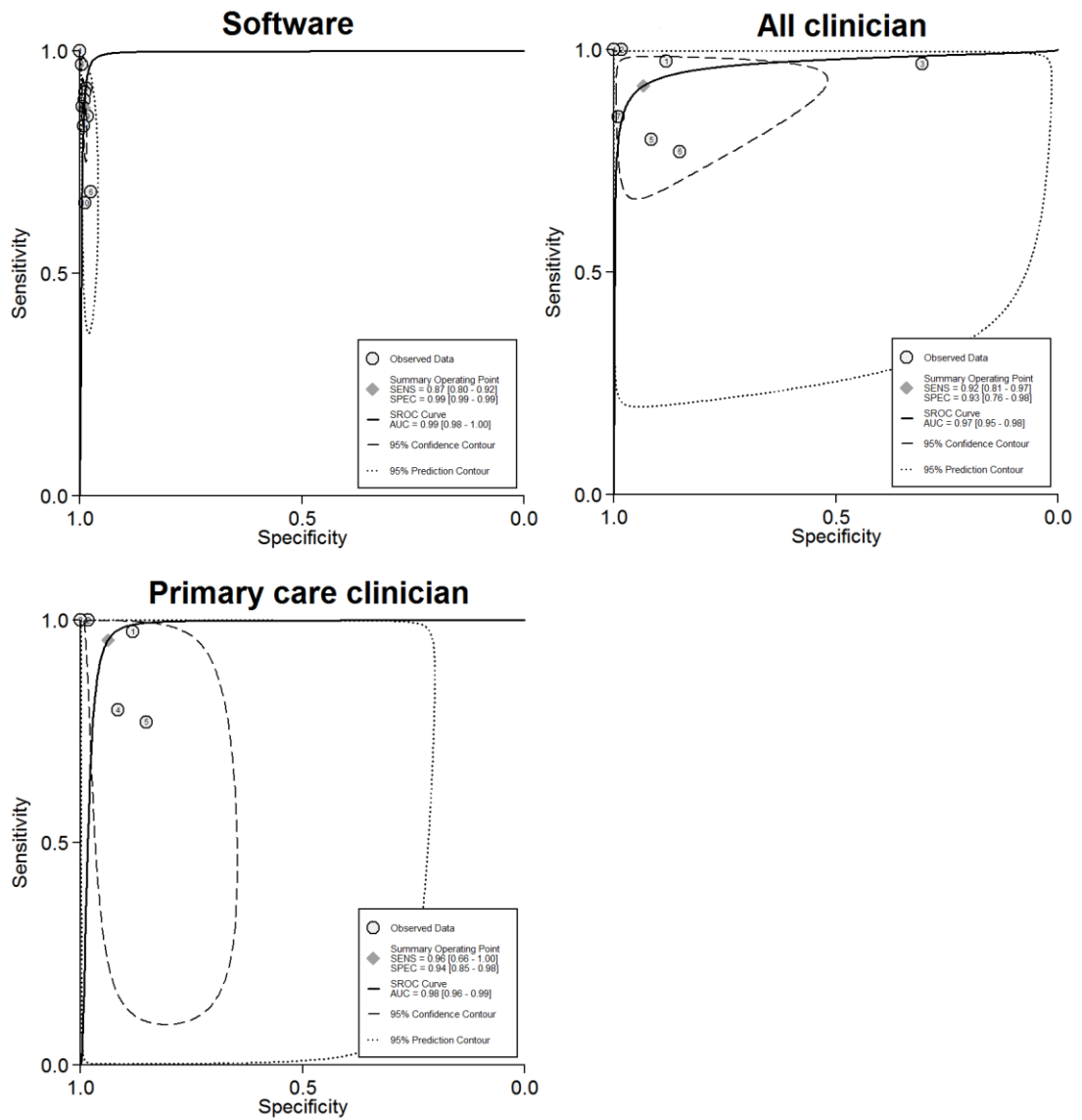
5.5.6. Sub-group analyses

The sub-group analyses for categories of GPs and nurses (figure 5-7) suggest the accuracy of primary care clinician diagnosed AF may be driven by a greater specificity of GPs' AF diagnoses than nurses [GPs: sensitivity 0.91 (95% C.I 0.68-1.00); specificity 0.96 (95% C.I 0.89-1.00); nurses: sensitivity 0.88 (95% C.I 0.63-1.00); specificity 0.85 (95% C.I 0.83-0.87)].

Bivariate sub-group analyses were similar after exclusion of studies with the lowest (D-grade) quality [Software: sensitivity 0.82 (95% C.I 0.73-0.88), specificity 0.99 (95% C.I 0.98-0.99); any healthcare professionals: sensitivity 0.92 (95% C.I 0.81-0.97), specificity 0.91 (95% C.I 0.70-0.98); any primary care professionals: sensitivity 0.93 (95% C.I 0.67-0.99), specificity 0.92 (95% C.I 0.85-0.96)].

5.5.7. Publication bias

There was no evidence of publication bias for studies of any clinician (p=0.29) or any primary care clinician diagnosis (p=0.19). However, studies of software ECG interpretation suggested the presence of publication bias (p=0.02), with the possible underrepresentation of smaller studies with a lower accuracy of diagnosing AF.

Figure 5-7: Sub-group analyses of the sensitivity and specificity of 12-lead ECG interpretation by GPs and practice nurses
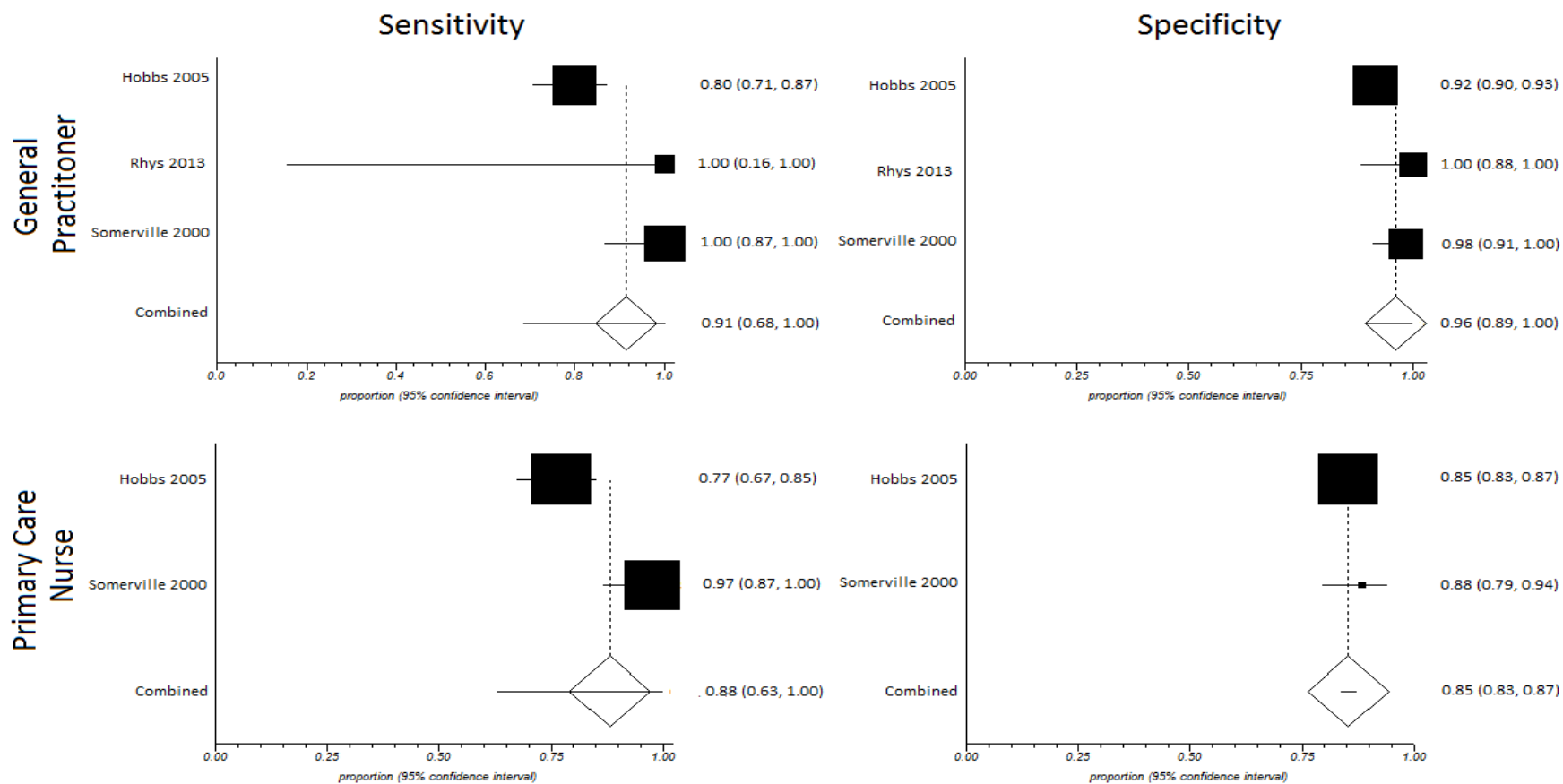
5.6. Discussion

5.6.1. Summary of principal findings

This systematic review found automated software and healthcare professional interpretation of 12-lead ECGs as methods for ECG interpretation in the diagnosis of AF. Of the 10 studies, only five were conducted in the UK. Most studies investigated automated software analysis of ECGs and were conducted in secondary care settings. Automated software analysis had a borderline greater specificity for AF diagnosis than healthcare professional interpretation of 12-lead ECGs. The sensitivities of automated software, any healthcare professionals and primary care professionals for interpreting 12-lead ECGs to diagnose AF were similar.

5.6.2. Strengths and limitations

To my knowledge, this study is the first systematic review and meta-analysis of different methods for interpreting 12-lead ECGs to diagnose AF. A strength of the study was the use of a standardised protocol that is consistent with published guidelines for systematic reviews of diagnostic test studies. Moreover, a comprehensive search strategy was used that included contacting authors of potentially relevant studies. The findings indicated a probable lack of publication bias for studies of clinicians' 12-lead ECG diagnoses of AF. However, there was the possibility of publication bias for

studies investigating automated software and this may limit the validity of the findings for this diagnostic modality.

One study was excluded due to the insufficient reporting of outcome data to enable meta-analysis and this could have influenced the findings. However, the number of overall misdiagnoses of AF was similar to that of other studies investigating the accuracy of automated software for making ECG diagnoses of AF and the impact of excluding this study is likely to be minimal.

Only one of the 10 included studies adopted a prospective design and there were a number of inherent methodological weaknesses in other studies as reflected by the appraisal of study quality. No studies were judged to have met all QUADAS-2 criteria and this was predominately due to the unclear reporting of study methods. This limits the internal validity of findings. However, the bivariate sub-group analyses that excluded studies judged to have the lowest (grade D) methodological quality found similar outcomes to the primary analyses, and supports these findings. Indeed, prospective higher quality studies would improve the internal validity of future research and provide greater confidence in the translation of findings to AF screening.

Most studies were conducted in a secondary care setting and there was substantial variation in the proportion of patients with AF. Healthcare professionals in secondary care are more likely to encounter patients with cardiovascular disease and may have greater experience in conducting and interpreting ECGs. Consequently the weight of evidence limits the generalisability and translation of review findings to unselected primary care settings that AF screening is intended for. However, the method of automated software to interpret ECGs is not reliant on clinical expertise and the findings for this method are likely to be transferable to primary care settings.

There was heterogeneity amongst the studies within all categories of methods for diagnosing AF and this is likely to be attributable to differences in study populations. Heterogeneity was greatest for the category of any healthcare professionals' interpretation of 12-lead ECGs and is likely to arise from differences in professional groups and clinical expertise (e.g. healthcare professionals in primary and secondary care). This variation was least for studies of automated software and strengthens the internal validity of findings for this approach to AF diagnosis.

5.6.3. Findings in context of previous research

The current gold-standard test for diagnosing AF is 12-lead ECG, (51, 108) and consensus recommends competent healthcare professionals should interpret this as part of AF screening. (51, 80, 108) Both systematic and opportunistic screening for AF using 12-lead ECG in patients over 65 years were found to be an effective approach for improving the detection of this arrhythmia. (118)

Harris et al. conducted a narrative literature review of studies from 2006 onwards to inform the Royal College of Physicians about how to best detect AF. (148) Harries et al. only identified four studies that reported outcomes for the accuracy of methods for interpreting 12-lead ECGs. (148) The review by Harris et al. identified GP, nurse and automated software methods for interpreting ECGs and the range of sensitivities and specificities were broad for all methods [GPs (n=2 studies): sensitivity 80-100% and specificity 92-98%; nurses (n=2 studies): sensitivity 77-97% and specificity 85-88%; automated software (n=2 studies): sensitivity 83-91% and specificity 91%]. This review, however, did not provide point estimates for the diagnostic accuracies or compare the accuracies of different methods for ECG interpretation, and the risk of bias of included studies were not appraised. (148) Therefore, the internal validity of findings from the review by Harris et al. are limited and my systematic review

provides up-to-date evidence with greater internal validity within findings.

My review identified automated software and healthcare professional interpretation of 12-lead ECGs as methods for diagnosing AF. Furthermore, the interpretation of ECGs in a restricted group of primary care professionals was also analysed. The findings for automated software, using sensitivity and specificity as measures of diagnostic accuracy, are consistent with those from the SAFE sub-study. (118, 119, 188) Due to the significantly higher specificity of this diagnostic modality, my findings suggest software is the best method for correctly identifying patients with normal 12-lead ECGs whilst minimising the risk of false positive diagnoses of AF.

Review findings also suggested the sensitivities of all methods for diagnosing AF were similar, although these may be sufficiently low to give rise to false negative AF diagnoses in clinical practice. As compared to any healthcare professionals' ECG interpretation, the point estimates for sensitivity were similar for AF diagnoses made by primary care professionals. However, the sub-group analyses suggested this may be attributable to better 12-lead ECG interpretation by GPs; in comparison to GPs, nurses were found to have a significantly lower specificity for diagnosing AF. Although

data from the SAFE trial, the largest, pragmatic study of AF screening in primary care, (118) were included in the review it is possible that the pooled estimates for diagnostic accuracy in the review have been over-estimated. Practices that undertake cardiovascular research in primary care may be self-selecting with an interest in AF and it is possible that the accuracy of diagnosing arrhythmias by primary care professionals in routine clinical practice could be lower than that found in my review.

5.7. Conclusions

Automated software had the greatest specificity for AF diagnosis using 12-lead ECG than healthcare professional diagnosis of this arrhythmia. Although the accuracy of diagnosing AF in primary care may be reassuring, this is driven by GP's diagnosis of AF. If a national AF screening programme is introduced into primary care it is possible that the skills of GPs and nurses for making 12-lead ECG diagnoses of AF would need improving to ensure the effectiveness of screening is not undermined.

This study investigated and compared the accuracies of different methods that could be used for the second-step of proposed AF screening. In the next chapter, I will investigate the feasibility of introducing AF screening within GP practices and the views of

healthcare professionals in this setting about their abilities to undertake screening activities.

Chapter 6. Survey of healthcare professionals in primary care about AF screening

6.1. Background

Although AF screening has been recommended, and a likely setting for any screening programme would be in primary care, the feasibility of introducing AF screening within this setting has not been established.

National screening programmes require quality assurance of screening procedures to ensure standards are met and both the effectiveness of screening is maintained whilst patient safety upheld. (195) This includes ensuring screening is delivered by healthcare professionals who are appropriately trained, qualified and competent. (195)

The effectiveness of AF screening is dependent upon accurate 12-lead ECG interpretation for diagnosing AF. (51, 80, 108) Studies that have evaluated the competencies of healthcare professionals in primary care to accurately interpret ECGs have focussed objectively on the skills of GPs. (196-198) Survey data suggest there is substantial variation in the accuracy of correctly interpreting ECGs, (197) with only 67% of GPs correctly identifying ECGs as normal and 65% correctly diagnosing AF. (197) Moreover,

another study of the accuracy of 12-lead ECG interpretation for any cardiac abnormalities found, as compared to cardiologist ECG interpretation, the sensitivity and specificity of GP diagnoses were 69.8% and 85.7%, respectively. (196) It is therefore conceivable that prior to screening implementation, the knowledge and skills of GPs to interpret 12-lead ECGs would need improving. It is also likely that other healthcare professionals, such as practice nurses, may have a role in future AF screening as studies have involved nurses in undertaking screening activities (e.g. performing pulse palpation and ECGs). (119, 137, 177)

It is still unclear whether GPs and other primary care professionals feel adequately skilled and if they are prepared to improve their skills, and whether they have the appropriate facilities to acquire and interpret ECGs. Therefore, understanding current practise and the views of healthcare professionals in primary care about AF screening are important priorities before considering its implementation. This would enable greater understanding of the perceived knowledge, skills and attitudes of those expected to undertake AF screening specific activities, such as performing and interpreting ECGs. This would also enable the identification of important facilitators, barriers and training needs of key stakeholder groups in order to deliver safe and effective screening.

To date, there have been no studies that have investigated the views of healthcare professionals in General Practice about the potential implementation of AF screening and their perceived abilities to undertake screening related activities.

6.2. Aims

To determine existing methods used for detecting AF within General Practices in the UK, and to determine and compare the knowledge, skills and attitudes, (KSA) and opinions of healthcare professionals (HCPs) about AF screening within this setting.

6.3. Objectives

- To determine the current practise for detecting pulse irregularities attributable to AF and diagnosing AF using 12-lead ECG in UK General Practice.

- To determine the knowledge, skills and attitudes of HCPs in primary care with respect to identifying patients with an irregular pulse and making 12-lead ECG diagnoses of AF.

- To determine the learning needs (current training and potential training requirements) of HCPs in primary care with respect to identifying patients with an irregular pulse and making 12-lead ECG diagnoses of AF, and to determine opinions about how these could be improved.

- To identify any foreseeable barriers experienced by HCPs to detecting and diagnosing AF in primary care.

6.4. Methods

The survey protocol was designed and written by JT. JT developed the survey, conducted the analyses and wrote the report. MJ supported JT in survey dissemination and data collection.

6.4.1. Study approach and participants

Surveys are a time-efficient approach of ascertaining large quantities of data, conveniently, from a large cohort of people. (199) As the aims and objectives of the study were broad and involved different professional groups across multiple sites, a cross-sectional survey of HCPs in Nottingham City Clinical Commissioning Group (CCG) was deemed an appropriate methodological approach and was conducted between October-December 2014 (Appendix 4). This was based on the assumption that screening would be conducted in a primary care setting. As there has been very little research investigating the views of HCPs in primary care about AF screening, conducting a survey in one CCG was considered a reasonable starting point to provide an initial understanding of this research theme. A census-sampling frame was deemed appropriate and feasible for the target population (i.e. all HCPs in Nottingham City CCG were surveyed). (200) Combined methods, using postal and web-survey, were used to maximise response rates, reduce the effects of non-responder

bias, and to improve the time and cost-efficiency of the survey. (200)

Nottingham City CCG comprised 67 inner-city GP practices serving 340,000 patients; (201) although the CCG has similar prevalences of long-term conditions to national estimates, there is greater mortality from cardio-respiratory diseases and greater potential years of life lost from causes amenable to healthcare than average estimates for England. (202)

Prior to survey implementation, information from on-line public resources and Nottingham City CCG were used to create a list of HCPs working at each practice. Eligible participants were GPs, nurses (nurses or nurse practitioners) and healthcare assistants (HCAs). Non-permanent staff (e.g. locum doctors) were not included. Practice managers were then contacted by telephone to check record accuracy. The final triangulated list of eligible participants was used as the denominator for survey responses. (199)

6.4.2. Survey design and implementation

6.4.2.1. Survey questions

6.4.2.1.1. Participant characteristics

Participant characteristics were ascertained for professional group, the number of years practising as a HCP, whether participants worked full-time (number of days worked in those not working full-time), if ECG training had been received since graduation and the time since training in those previously receiving ECG training (Appendix 4).

6.4.2.1.2. Existing methods for diagnosing atrial fibrillation and participant knowledge, skills and attitudes about atrial fibrillation screening

As current recommendations advocate two-step AF screening, using pulse palpation followed by 12-lead ECG in those with suspected AF, the survey questions ascertained information about existing methods for detecting and diagnosing AF, with a focus on pulse palpation, conducting and interpreting ECGs. Likert scale questions were developed to ascertain information about existing methods for detecting and diagnosing AF, and participant knowledge, skills and attitudes (KSA) for AF screening activities. The survey also included questions to ascertain participant views on training needs and potential roles in future AF screening.

The domains of KSA were used to assess the perceived abilities of HCPs to undertake screening activities as these directly relate to Bloom's taxonomy of learning objectives and can also be mapped to Millers Pyramid of educational theory for developing clinical competencies. (203)

Ordered Likert scale questions were used as they enable the efficient completion of multiple questions as part of a survey, enable the structured analysis of responses, enable comparisons between groups to be easily made and, if designed appropriately, are easy to navigate by respondents. (200) The number of ordinal points is an important consideration when designing survey Likert scale questions; too many options results in clustering of responses around certain points on the scale and too few points results in skipping of response items or marking of two adjacent answers. (200, 204) It has been suggested that Likert scales have optimal reliability and validity when 5-7 points are used, for bidirectional scales, and 3-5 points used for unidirectional scales. (200, 204) Therefore, this survey consisted predominately of three and five-point Likert scale closed questions for unidirectional and bidirectional questions, respectively (Appendix 4). Bidirectional scales used centrally placed neutral responses to provide balance within scales. (200)

6.4.2.1.3. Facilitators and barriers to atrial fibrillation screening

Barriers and training related facilitators for AF screening were ascertained using a combination of Likert scale questions (as above) and open questions requiring free-text responses (Appendix 4). This enabled deeper understanding of participant beliefs, attitudes and motivation within these contexts. (200) Open questions used were: 'Are there any specific areas about the diagnosis of AF using 12-lead ECGs that you would like training?' 'If such a screening program was introduced, what further training would you need to be able to undertake this role?' 'If a screening program for AF was introduced, are there any problems you think might prevent it working effectively at your surgery?'

6.4.2.2. Survey piloting

Piloting surveys is an essential component to survey design and improves the comprehensibility, face validity, participant burden, layout and the skip patterns used in surveys. (199) The survey was therefore piloted on HCPs from a different CCG than the intended population (five GPs, four Nurses and one HCA) and only minor modifications were subsequently required.

6.4.3. Survey dissemination

To improve response rates the survey was disseminated using an approach advocated by Dillman et al. and Safdar et al. (199, 200) Postal contact was made before survey implementation to inform individual participants about the research. A postal survey was then sent to all individuals; a web-link was also provided to enable on-line completion, if preferred. Two postal reminders (after four and eleven weeks from initial survey dissemination) were sent to non-responders. To promote greater awareness and further improve response, the research team attended two CCG led practice learning time events during the survey period to promote the survey.

6.4.4. Statistical analysis

Analyses were conducted using Stata version 11.0.

There have been no studies that investigate and compare the views of HCPs in primary care about AF screening. Consequently, there were no data to inform sample size calculations. Moreover, as this study was an initial exploration of views by HCPs, a power calculation was deemed unnecessary and data from this study could be used to inform future research design.

Participants were anonymised and given a unique ID code; this enabled monitoring and the identification of duplicate survey

responses; in cases where duplicate surveys were submitted it was pre-planned to contact participants to clarify any discordant responses.

Responses to survey questions, stratified by professional group, were summarised using proportions for categorical data and mean (SD) for parametric data, respectively. GPs have a lead role in practice management and are likely to have the most accurate knowledge of existing methods for detecting AF; for questions that related to existing methods of diagnosing AF within the practice, analyses were therefore conducted at a practice level and used only GP responses. Remaining questions were analysed within HCP occupation categories ascertained from the survey (GPs, nurses, nurse practitioners (NPs) and HCAs). NPs are registered nurses that work at a level well beyond initial registration with greater competencies and autonomy in patient care. (205)

Differences in participant characteristics across HCP groups were determined using chi-squared test, for categorical data, and analysis of variance (ANOVA) for parametric continuous data. Participant responses to questions about KSA to AF screening were summarized using proportions and 95% confidence intervals (CI) within HCP categories and allowed for the effects of clustering by practice using robust standard errors. Significance of associations

between HCP groups was determined, when cell sizes were sufficient, using logistic or multinomial regression, for dichotomous or categorical variables respectively.

Open-ended questions were read independently by one researcher (JT) and a thematic analytical approach was used to determine major themes for the barriers and facilitators for AF screening. (206)

6.4.5. Study ethics

Ethical approval was gained before survey piloting.

Implied consent was provided by participants through completion and submission of the survey; separate written or verbal consent was not obtained as implied consent was deemed appropriate and approved. Approval of study materials and procedures was granted by the University of Nottingham Research & Ethics Committee (REF: B11092014 14085 SoM PC) and Nottingham City CCG Research and Development (REF: 159703).

6.5. Results

6.5.1. Participant response

Participant response is shown in Fig 6-1. Of 67 practices registered within Nottingham City CCG, 59 were eligible for the survey; eight were excluded as they had closed, had no permanent staff, or shared staff with another practice. From 59 practices, there were 434 potentially eligible HCPs; 16 individuals were excluded because they were no longer employed by the CCG or had retired since initial contact was made. The final survey population was therefore 418 HCPs (229 GPs; 129 nurses; 60 HCAs). At least one GP responded from 48/59 (81%) practices; from all HCPs there were 212 (51%) respondents. [GPs: 52% (118/229); nurses: 52% (67/129); HCAs: 45% (27/60)]. Of the 67 nurse respondents, 17 were NPs. No duplicate surveys were returned.

Figure 6-1: Participant response to the survey
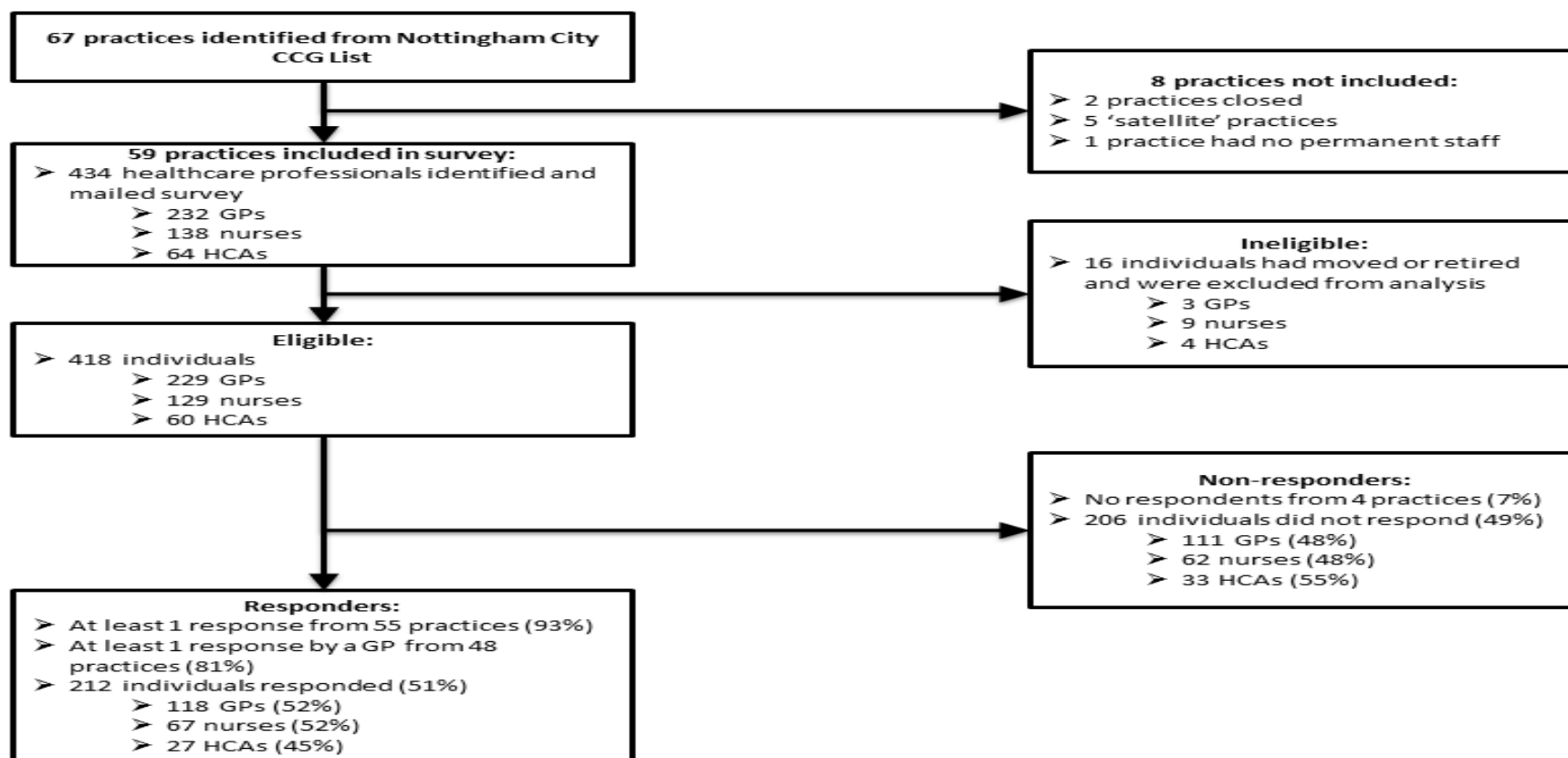
6.5.2. Participant characteristics

GPs had worked for a mean (SD) 20.1 (9.2) years and the time in practice was similar for nurses and NPs. HCAs had worked for a significantly shorter time (mean (SD) of 11.2 (8.5) years; $p<0.001$). Full-time working was similar across categories of HCPs. However, of participants working part-time, there were significant differences in the number of days worked across HCP groups; mean (SD) days worked were 3.1 (0.7), 3.8 (1.1), 3.5 (1.1) and 3.7 (0.8) for GPs, HCAs, nurses and NPs (p=0.009). Significantly more GPs (62.7%) and nurse practitioners (76.5%) received ECG training since graduation than nurses (50.0%) and HCAs (23.1%); p=0.005. However, of those receiving ECG training since graduation, a greater proportion of GPs (66.2%), HCAs (83.3%) and NPs (69.2%) received it within the last five years compared to nurses (28.0%); p=0.014.

6.5.3. Existing methods for diagnosing atrial fibrillation

From 48 practices with at least one GP respondent, 39 (81%) reported having an ECG machine. In practices without an ECG machine, all (100%) reported using another NHS GP practice to obtain ECGs and a few (12.5%) also used NHS hospitals. In practices with an ECG machine, HCAs and nurses (89.7% and 82.1% of practices, respectively) were most often reported as the HCPs responsible for conducting ECGs. GPs conducted ECGs in only

12.8% practices. 81.3% of practices reported diagnosing AF in-house and, in all those practices, GPs were responsible for making AF diagnoses. NPs were also reported to diagnose AF in 15.4% practices. Only 37.5% practices reported always diagnosing AF in-house. In practices that did not always make AF diagnoses most used other NHS services for this; 60% reported using an NHS hospital and 6.7% used other GP practices. 6.7% practices reported using private healthcare providers to diagnose AF and the remainder did not know or respond.

6.5.4. Knowledge, skills and attitudes (KSA) relating to atrial fibrillation screening

Table 6-1 presents the results for the knowledge and skills of HCPs for AF screening. There were no substantial differences between HCPs for performing pulse checks routinely and this was conducted by 95.8% GPs, 88.9% HCAs, 94.0% nurses and 100% NPs. There were no substantial differences in how often pulse checks were performed by HCPs although a greater proportion of NPs reported always undertaking this activity. However, fewer HCAs (33.3% (95% CI 18.2-52.9)) were confident at performing pulse checks than other HCP groups. A greater proportion of non-GP HCPs were confident at performing 12-lead ECGs than GPs [Proportion (95% CI) for HCAs: 77.8% (56.7-90.4); nurses: 70.0% (54.4-82.0); NPs: 94.1% (66.0-99.2); GPs: 33.1% (23.7-44.0)]. Fewer nurses

and HCAs were confident at diagnosing AF using 12-lead ECG than GPs and NPs.

Only 29.6% (95% CI 14.7-50.6) HCAs reported having excellent knowledge about identifying an irregular pulse, which was lower than other HCP groups [proportion (95% CI) for GPs 48.3 (38.7-58.1); nurses: 46.0 (32.4-60.2); NPs 76.5 (46.5-92.4)]. Fewer non-GP HCPs reported having excellent or good knowledge for interpreting abnormal 12-lead ECGs, diagnosing and treating AF than GPs.

Table 6-1: Knowledge and skills in conducting atrial fibrillation screening actives by healthcare professionals

Question	Response	GP (N=118)		Healthcare assistant (N=27)		Nurse (N=50)		Nurse practitioner (N=17)		P-value
		N (%)*	95% C.I*	N (%)*	95% C.I*	N (%)*	95% C.I*	N (%)*	95% C.I*	
Pulse checks										
Perform pulse checks	Yes	113 (95.8)	89.9-98.3	24 (88.9)	69.3-96.7	47 (94.0)	82.3-98.1	17 (100.0)	-	0.210
	No	4 (3.4)	1.2-8.9	3 (11.1)	3.4-30.7	3 (6.0)	1.9-17.0	0 (0.0)	-	
How often pulse check performed	Always	24 (20.3)	13.4-29.6	10 (37.0)	20.4-57.5	13 (26.0)	15.9-39.4	10 (58.8)	35.2-78.9	<0.001
	Often	64 (54.2)	45.5-62.7	7 (25.9)	11.2-49.2	24 (48.0)	35.5-60.8	6 (35.3)	19.3-55.5	
	Sometimes	23 (19.5)	13.2-27.8	7 (25.9)	12.0-47.2	10 (20.0)	11.8-31.9	1 (5.9)	0.9-31.9	
	Rarely	1 (0.8)	0.1-6.2	0 (0.0)	-	0 (0.0)	-	0 (0.0)	-	
Confidence in performing screening activities										
Identifying an irregular pulse	Very confident	99 (83.9)	77.0-89.0	9 (33.3)	18.2-52.9	36 (72.0)	55.6-84.1	17 (100.0)	-	n/a
	Somewhat confident	18 (15.3)	10.1-22.2	14 (51.9)	32.5-70.7	12 (24.0)	12.7-40.6	0 (0.0)	-	
	Not confident at all	0 (0.0)	-	3 (11.1)	3.8-28.5	1 (2.0)	0.3-13.9	0 (0.0)	-	
Performing 12-lead ECG	Very confident	39 (33.1)	23.7-44.0	20 (77.8)	56.7-90.4	35 (70.0)	54.4-82.0	16 (94.1)	66.0-99.2	<0.001
	Somewhat	53	35.3-54.9	3	3.4-30.7	10	10.8-34.0	1	0.8-34.0	

	confident	(44.9)		(11.1)		(20.0)		(5.9)		
	Not confident at all	25 (21.2)	15.4-28.5	2 (7.4)	1.7-26.6	4 (8.0)	2.9-20.0	0 (0.0)	-	
Deciding if ECG shows AF	Very confident	65 (55.1)	46.1-63.8	0 (0.0)	-	5 (10.0)	4.5-20.8	5 (29.4)	10.5-59.6	<0.001
	Somewhat confident	50 (42.4)	33.6-51.6	5 (18.5)	8.4-35.9	19 (38.0)	25.9-51.8	5 (29.4)	12.5-54.8	
	Not confident at all	1 (0.8)	0.1-6.1	19 (74.1)	56.0-86.5	25 (50.0)	36.3-63.7	7 (41.2)	19.5-66.9	
Knowledge of performing screening activities										
Identifying an irregular pulse	Excellent	57 (48.3)	38.7-58.1	8 (29.6)	14.7-50.6	23 (46.0)	32.4-60.2	13 (76.5)	46.5-92.4	n/a
	Good	58 (49.2)	39.4-59.0	11 (40.7)	21.7-63.0	24 (48.0)	35.5-60.8	4 (23.5)	7.6-53.5	
	Fair	2 (1.7)	0.4-6.7	5 (22.2)	9.5-43.9	2 (4.0)	1.0-14.5	0 (0.0)	-	
	Poor	0 (0.0)	-	1 (3.7)	0.5-23.5	0 (0.0)	-	0 (0.0)	-	
	Non-existent	0 (0.0)	-	0 (0.0)	-	0 (0.0)	-	0 (0.0)	-	
Deciding the cause of an abnormal 12-lead ECG	Excellent	7 (5.9)	2.8-12.0	0 (0.0)	-	1 (2.0)	0.3-13.9	2 (11.8)	3.0-36.4	<0.001
	Good	56 (47.5)	38.8-56.3	1 (3.7)	0.6-20.7	6 (12.0)	4.9-26.4	3 (17.6)	5.8-42.6	
	Fair	48 (40.7)	31.2-50.9	5 (18.5)	6.8-41.6	17 (34.0)	22.9-47.2	5 (29.4)	13.6-52.4	
	Poor	5 (4.2)	1.5-11.7	7 (25.9)	13.5-44.0	17 (34.0)	21.4-49.3	7 (41.2)	21.9-63.7	
	Non-existent	0 (0.0)	-	12 (44.4)	26.5-63.9	8 (16.0)	6.6-34.0	0 (0.0)	-	
Deciding if 12-lead ECG shows AF	Excellent	31 (26.3)	17.8-37.0	0 (0.0)	-	1 (2.0)	0.3-12.9	2 (11.8)	2.7-38.8	n/a

		N (%)	95% C.I	N (%)	95% C.I	N (%)	95% C.I	N (%)	95% C.I	p-value
	Good	74 (62.7)	51.5-72.7	3 (11.1)	2.5-37.8	8 (16.0)	8.3-28.7	6 (35.3)	15.3-62.3	
	Fair	11 (9.3)	4.7-17.8	7 (25.9)	13.5-44.0	20 (40.0)	29.6-51.4	4 (23.5)	9.9-46.4	
	Poor	0 (0.0)	-	5 (18.5)	7.3-39.6	15 (30.0)	18.4-44.8	4 (23.5)	9.0-48.8	
	Non-existent	0 (0.0)	-	9 (33.3)	16.9-55.1	5 (10.0)	4.1-22.3	1 (5.9)	0.8-34.0	
Deciding on treatment for AF	Excellent	20 (16.9)	9.9-27.4	0 (0.0)	-	0 (0.0)	-	1 (5.9)	0.8-34.0	<0.001
	Good	66 (55.9)	46.3-65.2	1 (3.7)	0.5-23.5	8 (16.0)	7.7-30.3	4 (23.5)	7.1-55.4	
	Fair	27 (22.9)	16.1-31.5	1 (3.7)	0.5-22.1	12 (24.0)	13.8-38.4	4 (23.5)	9.0-48.8	
	Poor	2 (1.7)	0.4-7.0	3 (14.8)	5.6-34.0	16 (32.0)	20.0-47.0	6 (35.3)	15.3-62.3	
	Non-existent	1 (0.8)	0.1-6.1	19 (70.4)	47.3-86.3	12 (24.0)	12.9-40.2	2 (11.8)	2.7-38.8	

*N=number of participants responding to question item; %=proportion of participants, adjusted for clustering by practice; 95% C.I= 95% confidence interval for the proportion of participants; n/a=unable to calculate p-value to insufficient data within cells
Missing data within question responses is present when the sum of column percentages <100%

189

Attitudes of HCPs about training for AF screening are presented in Table 6-2. More HCAs (48.1% (95% CI 30.6-66.2)) felt they would benefit from pulse palpation training than other HCPs (proportion (95% CI) for GPs: 7.6% (3.6-15.3); nurses: 18.0% (8.5-34.0); NPs: 0%]. All categories of HCPs felt they would benefit from ECG interpretation training, however, and there were no substantial differences between professional groups. However, a greater proportion of non-GP HCPs reported they would benefit from ECG interpretation training specifically for AF than GPs [proportion (95% CI) for GPs: 11.9% (6.8-20.0); HCAs: 37.0% (21.7-55.5); nurses: 44.0% (30.0-59.0); NPs 41.2% (21.9-63.7)]. More non-GP HCPs also felt they would be better at diagnosing AF if they received ECG interpretation training than GPs. Similar proportions of participants strongly agreed they would like to receive general ECG training across professional groups. However, more non-GP HCPs strongly agreed they would like to receive ECG training specifically for AF than GPs [proportion (95% CI) for GPs: 13.6 (8.2-21.5); HCAs: 40.7% (24.2-59.7); nurses 38.0% (24.1-54.1); NPs: 29.4% (13.6-52.4); $p < 0.001$). In contrast, fewer HCAs, nurses and NPs wanted to be involved in diagnosing AF than GPs.

Table 6-2: Attitudes of healthcare professionals about training for atrial fibrillation screening

Question	Response	GP (N=118)		Healthcare assistant (N=27)		Nurse (N=50)		Nurse practitioner (N=17)		P-value
		N (%)*	95% C.I*	N (%)*	95% C.I*	N (%)*	95% C.I*	N (%)*	95% C.I*	
Benefit from pulse palpation training	Strongly agree	9 (7.6)	3.6-15.3	13 (48.1)	30.6-66.2	9 (18.0)	8.5-34.0	0 (0.0)	-	n/a
	Agree	16 (13.6)	8.2-21.6	9 (33.3)	18.2-52.9	17 (34.0)	22.3-48.1	1 (5.9)	0.8-34.0	
	Not sure	16 (13.6)	8.5-21.0	0 (0.0)	-	5 (10.0)	4.3-21.5	3 (17.6)	5.8-42.6	
	Disagree	56 (47.5)	38.0-57.1	1 (3.7)	0.5-23.5	14 (28.0)	16.8-42.9	8 (47.1)	25.9-69.3	
	Strongly disagree	19 (16.1)	10.5-23.9	1 (3.7)	0.6-20.7	4 (8.0)	3.1-18.9	5 (29.4)	12.5-54.8	
Benefit from ECG interpretation training	Strongly agree	37 (31.4)	23.1-50.0	15 (55.6)	37.0-72.7	25 (50.0)	35.8-64.2	10 (58.8)	36.3-78.1	n/a
	Agree	60 (50.8)	41.3-60.4	6 (22.2)	10.9-40.0	17 (34.0)	21.6-49.0	5 (29.4)	13.6-52.4	
	Not sure	7 (5.9)	3.3-10.6	2 (7.4)	1.0-38.9	3 (6.0)	2.0-16.7	0 (0.0)	-	
	Disagree	8 (6.8)	3.1-14.3	2 (7.4)	1.7-26.6	2 (4.0)	1.0-14.9	2 (11.8)	2.7-38.8	
	Strongly disagree	4 (3.4)	1.3-8.4	0 (0.0)	-	2 (4.0)	1.0-15.2	0 (0.0)	-	
Benefit for ECG interpretation training for AF	Strongly agree	14 (11.9)	6.8-20.0	10 (37.0)	21.7-55.5	22 (44.0)	30.0-59.0	7 (41.2)	21.9-63.7	<0.001
	Agree	38 (32.2)	25.3-40.0	9 (33.3)	18.2-52.9	17 (34.0)	21.3-49.4	7 (41.2)	21.1-64.7	
	Not sure	15 (12.7)	8.1-19.3	5 (18.5)	6.5-42.6	3 (6.0)	2.0-16.7	2 (11.8)	2.7-38.8	
	Disagree	42 (35.6)	27.2-44.9	1 (3.7)	0.5-23.5	5 (10.0)	4.3-21.5	1 (5.9)	0.83-4.0	

	Strongly disagree	7 (5.9)	3.0-11.4	0 (0.0)	-	2 (4.0)	1.015.2	0 (0.0)	-	
Better at diagnosing AF if received ECG interpretation training	Strongly agree	20 (16.9)	10.7-25.7	11 (40.7)	24.6-59.1	19 (38.0)	24.5-53.7	7 (41.2)	21.9-63.7	<0.001
	Agree	31 (26.3)	19.6-34.2	5 (18.5)	7.7-38.2	20 (40.0)	27.2-54.4	8 (47.1)	25.9-69.3	
	Not sure	22 (18.6)	11.3-29.2	5 (18.5)	7.0-40.7	4 (8.0)	2.9-20.4	1 (5.9)	0.8-34.0	
	Disagree	35 (29.7)	21.1-39.9	2 (7.4)	1.7-26.6	3 (6.0)	1.9-17.0	1 (5.9)	0.8-34.0	
	Strongly disagree	8 (6.8)	3.5-12.7	1 (3.7)	0.5-23.5	3 (6.0)	1.9-17.0	0 (0.0)	-	
Would like ECG training (any condition)	Strongly agree	37 (31.4)	23.9-39.9	12 (44.4)	27.3-63.0	21 (42.0)	28.1-57.3	11 (64.7)	44.5-80.7	n/a
	Agree	61 (51.7)	42.5-60.8	6 (22.2)	10.9-40.0	16 (32.0)	19.2-48.2	5 (29.4)	14.9-49.8	
	Not sure	8 (6.8)	3.5-12.8	2 (7.4)	1.7-26.6	5 (10.0)	3.7-24.0	0 (0.0)	-	
	Disagree	7 (5.9)	2.9-11.8	3 (11.1)	2.5-37.8	3 (6.0)	1.9-17.4	1 (5.9)	0.8-34.0	
	Strongly disagree	3 (2.5)	0.9-7.3	0 (0.0)	-	4 (8.0)	3.1-19.3	0 (0.0)	-	
Would like ECG training (AF)	Strongly agree	16 (13.6)	8.2-21.5	11 (40.7)	24.2-59.7	19 (38.0)	24.1-54.1	5 (29.4)	13.6-52.4	<0.001
	Agree	33 (28.0)	21.4-35.6	7 (25.9)	13.5-44.0	14 (28.0)	17.3-42.0	9 (52.9)	31.0-73.8	
	Not sure	21 (17.8)	11.5-26.5	3 (11.1)	3.6-29.7	5 (10.0)	4.6-20.4	2 (11.8)	2.7-38.8	
	Disagree	38 (32.2)	23.1-42.8	2 (7.4)	1.8-25.4	8 (16.0)	8.3-28.7	1 (5.9)	0.8-34.0	
	Strongly disagree	8 (6.8)	3.4-13.2	0 (0.0)	-	3 (6.0)	1.9-17.0	0 (0.0)	-	
Would like to be	Strongly	32	19.5-36.4	6	10.0-42.3	12	14.2-37.6	8	26.2-69.0	<0.00

involved in diagnosing AF	agree	(27.1)		(22.2)		(24.0)		(47.1)		1
	Agree	61 (51.7)	43.8-59.5	3 (11.1)	3.6-29.7	10 (20.0)	11.0-33.6	2 (11.8)	3.0-36.4	
	Not sure	8 (6.8)	3.0-14.5	6 (22.2)	9.8-42.8	14 (28.0)	16.5-43.3	6 (35.3)	17.6-58.1	
	Disagree	9 (7.6)	3.9-14.4	4 (14.8)	5.6-34.0	10 (20.0)	10.3-35.1	1 (5.9)	0.9-31.1	
	Strongly disagree	2 (1.7)	0.4-6.9	4 (14.8)	5.8-32.9	3 (6.0)	1.9-17.0	0 (0.0)	-	

*N=number of participants responding to question item; %=proportion of participants, adjusted for clustering by practice; 95% C.I= 95% confidence interval for the proportion of participants; n/a=unable to calculate p-value to insufficient data within cells

Missing data within question responses is present when the sum of column percentages <100%

6.5.5. Facilitators and barriers to AF screening

6.5.5.1. Quantitative results

HCPs views on their potential roles in AF screening are presented in Table 6-3. Most participants reported having a likely role in performing pulse checks although a greater proportion of nurses and NPs reported having this role than other HCPs. More nurses and NPs also reported being very likely to have a role in conducting 12-lead ECGs [proportion (95% CI) for GPs: 31.4% (23.1-41.0); HCAs: 48.1% (30.4-66.4); nurses: 70.0% (52.7-83.0); NPs 64.7% (39.9-83.5)]. Fewer non-GP HCPs reported having a future role in ECG interpretation and AF diagnosis than GPs.

Table 6-3: Perceived role of healthcare professionals in future atrial fibrillation screening

Question	Response	GP (N=118) N (%)*	GP 95% C.I*	Healthcare assistant (N=27) N (%)*	Healthcare assistant 95% C.I*	Nurse (N=50) N (%)*	Nurse 95% C.I*	Nurse practitioner (N=17) N (%)*	Nurse practitioner 95% C.I*	P-value
Role in performing pulse checks	Very likely	61 (51.7)	41.0-62.2	12 (44.4)	27.6-62.7	42 (84.0)	72.5-91.3	12 (70.6)	44.4-87.8	n/a
	Likely	37 (31.4)	22.9-41.3	7 (25.9)	11.2-49.2	6 (12.0)	5.8-23.3	2 (11.8)	1.6-52.3	
	Unsure	9 (7.6)	3.9-14.4	6 (22.2)	9.8-42.8	0 (0.0)	-	0 (0.0)	-	
	Unlikely	3 (2.5)	0.8-7.5	0 (0.0)	-	0 (0.0)	-	1 (5.9)	0.8-34.0	
	Very unlikely	3 (2.5)	0.8-22.2	0 (0.0)	-	0 (0.0)	-	0 (0.0)	-	
Role in conducting 12-lead ECGs	Very likely	37 (31.4)	23.1-41.0	13 (48.1)	30.4-66.4	35 (70.0)	52.7-83.0	11 (64.7)	39.9-83.5	n/a
	Likely	29 (24.6)	17.1-33.9	6 (22.2)	9.6-43.3	4 (8.0)	2.9-20.0	3 (17.6)	4.0-52.2	
	Unsure	6 (5.1)	2.3-11.0	4 (14.8)	6.1-31.7	4 (8.0)	3.0-19.3	0 (0)	-	
	Unlikely	27 (22.9)	16.4-31.0	0 (0)	-	1 (2.0)	0.3-13.4	1 (5.9)	0.8-34.0	
	Very unlikely	14 (11.9)	7.7-17.7	2 (7.4)	1.7-26.6	4 (8.0)	2.9-20.0	0 (0)	-	
Role in ECG interpretation for AF	Very likely	71 (60.2)	48.8-70.5	2 (7.4)	1.7-26.6	7 (14.0)	6.4-27.8	5 (29.4)	12.5-54.8	<0.001
	Likely	37 (31.4)	22.8-41.5	2 (7.4)	1.7-26.6	8 (16.0)	8.1-29.1	4 (23.5)	8.3-51.0	
	Unsure	6 (5.1)	2.3-10.8	9 (33.3)	18.9-51.7	18 (36.0)	24.4-49.5	3 (17.6)	5.8-42.6	
	Unlikely	0	-	6	9.8-42.8	9	10.5-29.0	3	4.0-52.2	

195

		N (%)	95% C.I	N (%)	95% C.I	N (%)	95% C.I	N (%)	95% C.I	p-value
		(0)		(22.2)		(18.0)		(17.6)		
	Very unlikely	0 (0)	-	6 (22.2)	10.4-41.1	6 (12.0)	5.4-24.5	0 (0)	-	
Role in diagnosing AF	Very likely	69 (58.5)	46.9-69.2	0 (0)	-	5 (10.0)	3.7-24.1	5 (29.4)	12.5-54.8	n/a
	Likely	40 (33.9)	24.8-44.4	1 (3.7)	0.5-23.5	6 (12.0)	5.2-25.2	3 (17.6)	5.3-44.9	
	Unsure	5 (4.2)	1.7-9.9	8 (29.6)	16.2-47.9	15 (30.0)	19.3-43.4	1 (5.9)	0.8-34.0	
	Unlikely	0 (0)	-	3 (11.1)	2.5-37.8	11 (22.0)	11.8-37.2	6 (35.3)	15.3-62.3	
	Very unlikely	0 (0)	-	13 (48.1)	30.5-66.3	11 (22.0)	12.0-36.8	0 (0)	-	

*N=number of participants responding to question item; %=proportion of participants, adjusted for clustering by practice; 95% C.I= 95% confidence interval for the proportion of participants; n/a=unable to calculate p-value to insufficient data within cells

Missing data within question responses is present when the sum of column percentages <100%

6.5.5.2. Findings from open-ended questions

There were 337 free-text responses from 171/212 (81%) respondents (105 GPs; 13 HCAs; 53 nurses). Around 20% responses identified no barriers to screening within current practice. Common themes for barriers, in all HCP groups, to AF screening were time to undertake screening, workload, lack of appointments, staffing levels within the practice, access to the required equipment, and available funding to conduct screening activities. [Comment 212 (GP): "we would require some form of extra resources to carry this out depending on the work required general practice is currently overstretched with work and conflicting demands"; Comment 219 (GP) "workload issues"; Comment 231 (GP): time, time, time, the waiting time for anticoagulation clinic would need to be reduced currently two to three weeks and GP carries responsibility for any adverse event; also who will find the money for new anticoagulants". Comment 311 (Nurse): "lack of appointments, too few nurses, extra load on all members of the team"]. Less common barriers included the perception that screening activities were not their current role, lack of space within the practice, lack of training, and the patient reluctance to screening.

Only 10% of responses suggested there were no facilitators required for screening to be implemented within existing practice.

The most common theme identified as a facilitator for screening was additional training requirements; commonly reported requirements were training for conducting and interpreting 12-lead ECGs, the management of AF and undertaking pulse palpation. [Comment 57 (GP): "brief ECG update training and advice on management of AF once diagnosed"; Comment 69 (GP): "Training for practice nurses in AF diagnosis/management; written protocol pathway to aid above process"; Comment 99 (GP): "Further training on ECG interpretation. I am fairly confident that I can identify AF on an ECG but looking at ECG uncovers other abnormalities that I have less confidence in my interpretation"; Comment 151 (Nurse): "ECG training reading and interpretation of results"]. Less common facilitators to screening included provision or access to 12-lead ECGs and guidelines on AF screening.

6.6. Discussion

6.6.1. Summary of principal findings

This survey found that, even in this inner-city area, most respondents from practices believe they are able to perform and interpret ECGs in-house and were potentially well-equipped for future AF screening. Non-GP HCPs reported having less knowledge about ECG interpretation and the treatment of AF than GPs. However, non-GP HCPs more frequently reported they would benefit from ECG training specifically for diagnosing AF. All HCP groups reported they would like to receive training in ECG interpretation but this was specifically for AF diagnosis in non-GP groups. However, non-GP HCPs did not perceive themselves to have a future role in ECG interpretation or AF diagnosis.

6.6.2. Strengths and limitations

To my knowledge, this is the first study to ascertain the readiness for and views of HCPs regarding the introduction of AF screening in General Practices.

A strength of this study was the high practice-level response rate: at least one GP responded from 81% of practices; therefore it is likely that representative estimates for existing methods for detecting AF within inner-city practices were ascertained. Whilst the response rate from individual participants was satisfactory

199

(51%) there is a possibility that non-respondents' knowledge, skills, attitudes and opinions might be different from those who completed questionnaires. For example, non-responders may have lower enthusiasm for AF screening and I may have overestimated HCP interest in this.

Although findings are likely to represent the views of HCPs within inner-city practices of Nottingham City CCG, another limitation of this study is the generalisability of findings to professionals in other primary care settings, such as those working in rural settings. The prevalence of long-term conditions and associated health problems experienced by patients in Nottingham City CCG is similar to national average estimates. (207) Moreover, in 2014 Nottingham City CCG had similar ratios of GPs and nurses to patient population as the England average. (208) This suggests the burden of long-term conditions and staffing available for managing these is similar to national estimates. Consequently, the views of HCPs in this study may be generalisable to professionals from other inner-city practices.

HCPs working in the same practice may have similar abilities to detect AF and share similar opinions about screening; such clustering effects could have influenced the findings from the survey. However, this was allowed for in the quantitative analyses

by adjusting for the effects of clustering by practice and, consequently, the findings for these survey questions are likely to have greater precision. There remains the possibility of residual confounding as factors, such as time since ECG training, were not adjusted for in the analyses and could influence the outcomes in either direction. It is likely, however, that such effects were accounted for when adjusting for the effects of clustering by practice as GP practices often have in-house training and quality assurance processes.

Although p-values were obtained to give an indication of true differences between HCP groups, the level of significance should be treated with caution given the number of statistical tests performed. Furthermore, this study was small in sample size and, combined with the lack of a power calculation, there is a limited ability to determine differences between HCPs groups.

The survey ascertained information about methods for detecting AF in accordance with current recommendations – pulse palpation and 12-lead ECG. (80) It is possible that some practices may be using other methods to detect patients with suspected AF (e.g. non-12-lead ECGs) and information regarding practise using newer technologies is not known.

Another limitation to the survey is that data were ascertained for the perceived abilities of HCPs to undertake screening activities and there were no direct comparisons with objective information for the abilities of HCPs to detect or diagnose AF. The findings from research undertaken in chapter five of this thesis suggest that primary care professionals may under diagnose AF when interpreting ECGs; it is therefore possible that survey participants could have overestimated their competencies at undertaking such activities.

Another limitation of this study was its cross-sectional design and the assumption that screening would be implemented within a primary care setting. The temporal relationship between HCPs views about screening and subsequent abilities to undertaken screening cannot be established.

Finally, the survey ascertained both quantitative and qualitative data for the views of HCPs about the future implementation of AF screening. Although findings were consistent between both approaches there are methodological limitations of using open-ended questions for qualitative data as part of a survey. Moreover, there were only three open-ended questions in the survey with limited space for free-text responses. The outcomes from open-ended questions are more likely to provide an indication of views

expressed rather than deeper understanding of the opinions of HCPs about AF screening. Although surveys are a time-efficient method of data acquisition, the lack of investigator at survey completion does not enable probing/clarification of uncertain responses. Face-to-face qualitative research would therefore provide a greater in-depth exploration of the themes identified from the survey.

6.6.3. Comparison with existing literature

There have been few studies that have investigated the feasibility of conducting ECGs in primary care. Begg et al. undertook a cross-sectional survey in the UK of HCPs in primary care (226 GPs, 13 GP registrars, five nurses) and secondary care physicians about ECG acquisition and interpretation. Of primary care respondents, 82% reported having an ECG machine at their practice and 82% reported nurses or HCAs as the HCP that performed ECGs. (209) These findings are consistent with the estimates from my survey and support the assertion that GP Practices are potentially well-equipped for delivering AF screening as they have good access to ECGs.

There have been very few studies that have investigated the competencies of HCPs in Primary Care for interpreting ECGs. Begg et al. also investigated the competencies of HCPs to interpret

ECGs. Survey participants were asked about their views about interpreting ECGs and they were provided six ECGs, with a variety of abnormalities, to interpret. (209) Approximately, 90% of HCPs in Primary Care interpreted less than five ECGs per week. Moreover, only 45% of respondents felt very or fairly confident at ECG interpretation but these findings were not provided according to professional groups. There was also substantial variation in the accuracy of ECG interpretation by Primary Care professionals. The findings by Begg et al. support the suggestion that training to improve the accuracy of ECG interpretation in Primary Care would be an important consideration if screening were implemented in this setting.

The limited competencies of HCPs in Primary Care to undertake screening activities is consistent with findings of studies from other screening programmes. Patel et al. conducted a web-based survey of 147 General Practice surgeries in the East Midlands, UK about the Human Papilloma Virus (HPV) vaccine as part of cervical screening. (210) The survey explored practice nurse knowledge and attitudes towards HPV vaccine and self-perceived adequacy of HPV knowledge. Patel et al. found that basic knowledge was lacking; 9.6% of respondents failed to identify HPV as a cause of cervical cancer and 62.8% nurses believed that HPV required treatment. Only 68% of nurses felt adequately informed about HPV

and the need to provide training was identified as an important facilitator to future screening. (210)

There have also been very few studies that have investigated the opinions of HCPs in primary care about AF screening implementation. Studies of AF case finding in pharmacies have found that screening using single-lead ECGs was acceptable by community pharmacists and that and there was enthusiasm for screening within this setting. (140, 144) Since conducting my survey, Orchard et al. have published their findings of a cross-sectional pilot study of AF screening. (211) Practice nurses from five GP practices in Australia screened patients using smart phone ECGs during influenza vaccination clinics. As part of this study, practice nurses (n=7), GPs (n=5) and practice managers (n=5) were interviewed to ascertain their views about AF screening implementation. (211) Practice nurses felt confident at performing screening and enjoyed the extra interaction with patients. (211) GPs and practice managers were also positive about screening implementation. However, all professional groups identified key barriers as time and capacity to undertake screening. (211)

The findings from the study by Orchard et al. and studies of screening implementation in pharmacies are consistent with the results of my survey where HCP groups were potentially

enthusiastic about screening but similar barriers to its implementation were identified.

6.7. Conclusions

Primary care is potentially well resourced and ready to deliver AF screening, with most healthcare professionals at surveyed practices perceiving they have the ability to detect pulse irregularities and perform 12-lead ECGs. Compared to GPs, other HCPs feel they have less knowledge and skills for interpreting 12-lead ECGs and diagnosing AF. Therefore GPs may be the appropriate professional group for diagnosing AF as part of screening. However, non-GP HCPs also reported they would like to gain skills in ECG interpretation. Therefore, nurses may have the greatest potential to up-skill and could have an important role in further supporting future AF screening.

Chapter 7. Summary and recommendations

7.1. Summary and implications

Screening for AF in primary care has been recommended; current guidance advocates using a two-stage approach for screening, where patients with pulse irregularities are identified and then AF is subsequently diagnosed or excluded using 12-lead ECG in those with suspected AF. (80, 108) The overall aim of this programme of research was to determine how AF screening might feasibly and effectively be introduced into primary care in the UK and research undertaken has progressed the understanding of this.

The first systematic review (chapter four) identified four methods - pulse palpation, non-12-lead ECGs, modified blood pressure monitors and smart phone devices - for identifying patients with pulse irregularities caused by AF, and found that pulse palpation had the lower accuracy for detecting suspected AF than other methods due to its lower specificity. Pulse palpation would therefore result in greater false positive cases of suspected AF and more patients unnecessarily requiring 12-lead ECG than other methods.

The findings from this review provide evidence on how the first-step of proposed AF screening may be better organised and support the use of newer technologies to detect patients with pulse

irregularities attributable to AF as alternatives to pulse palpation. Greater accuracy of new technologies would reduce the number of unnecessary ECGs subsequently conducted would have an impact on reducing service utilisation (conducting and interpreting ECGs) and potential psychological harm to patients that are falsely identified as having suspected AF. However, this study does not provide data for the effectiveness of new technologies to detect AF when compared to pulse palpation or the subsequent translation of findings to changes in stroke burden.

Pulse palpation is considered a cheap and feasible method for detecting patients with an irregular pulse. (148) Any other method of detecting pulse irregularities caused by AF should, in addition to being cheap, be accurate, quick and simple for it to be a cost-effective intervention in primary care. The review findings are supported by recent guidance from the National Institute for Health and Care Excellence (NICE) that advocate the use of an automated BP monitor for the detection of suspected AF in patients being screened or monitored for hypertension. (212) Modified blood pressure monitors were found to have a substantially greater accuracy for detecting pulse irregularities caused by AF than pulse palpation; such devices are likely to be a pragmatic alternative to pulse palpation as blood pressure checks are an integral component of existing cardiovascular screening programmes in

primary care. (213) Furthermore, automated devices would enable screening to be conducted by all healthcare professionals without the need for additional training, and could be used for all patients in the target screening population. However, to date there have been no economic analyses comparing alternative technologies to pulse palpation for detecting pulse irregularities attributable to AF and this would help to further inform optimal planning and service configurations of any future AF screening programme.

The first systematic review also highlighted the potential utility of smart phone applications for detecting irregular pulses caused by AF. This method was found to have a similar diagnostic accuracy as blood pressure monitors. However, there were only two studies investigating smart phone applications and both were small in sample size. In addition, one of these studies investigated multiple software algorithms with different thresholds to determine a positive test result using the same cohort of patients; this reduces the internal validity of findings and the precision of point estimates for diagnostic accuracy of smart phone applications. Therefore, the findings for this method of identifying suspected AF should be interpreted with caution. If these findings, however, are replicated in larger studies that are representative of those targeted by screening, this raises the future possibility of using such

technologies within both the clinic and home settings for detecting AF.

The second systematic review (chapter five) identified two methods - automated software and healthcare professional analysis - for interpreting 12-lead-ECGs for the diagnosis of AF. The review found that automated software analysis of ECGs had the greater specificity for AF diagnosis than healthcare professional ECG interpretation; software ECG interpretation would therefore result in the greatest number of true negative cases being identified and the lowest number of false positives.

However, the sensitivities of automated software and healthcare professional ECG interpretation were similar and substantially lower than the respective specificities. Therefore, all methods of ECG interpretation would potentially result in excessive false negative diagnoses of AF. Moreover, sub-group analyses found the accuracy of 12-lead-ECG interpretation in primary care was greater for GPs than nurses due to a lower specificity for nurse diagnosed AF.

The specificities of methods of ECG interpretation suggest automated software would be a better method for ruling in AF; using healthcare professional ECG interpretation alone would result in greater false positive diagnoses of AF than software interpretation. This would result in potential treatment related and psychological harm to patients that are incorrectly diagnosed with

AF and inappropriately receive stroke preventative treatments. The lower sensitivities of all ECG interpretation methods suggest that there is the potential for excess false negative diagnoses of AF and patients incorrectly having AF ruled out, thus remaining at risk of stroke. However, the review did not provide evidence for the impact the sensitivities and specificities from different interpretation methods on the effectiveness and cost-effectiveness of screening.

The findings from the second review also suggest the accuracy of interpreting ECGs and diagnosing AF in primary care would require improvement should screening be implemented within this setting. An alternative approach arising from the findings is the potential for combining software and healthcare professional interpretation of ECGs for the diagnosis of AF as part of screening. To date only one study has provided data for the accuracy of combining different methods for interpreting 12-lead-ECGs and diagnosing AF. (188) Mant et al. conducted secondary analyses of SAFE trial data and found that combining software and GP interpretation of 12-lead ECGs did not result in an improvement in the sensitivity of diagnosing AF. (188) This study, however, did not combine other healthcare professionals' (i.e. nurses) diagnoses of AF with interpretive software and so the accuracy of using other combinations for diagnosing AF is not known. The consistently high

specificity of automated software suggests it has potential utility for the triage of ECGs and exclusion of patients with normal ECG findings; this could be used to avoid physician interpretation of normal ECGs during AF screening, reducing the number of false positive diagnoses of AF. Furthermore, reducing the number of ECGs that require physician interpretation would also make screening more time efficient and potentially less costly. However, correctly diagnosing AF using software interpretation, either alone or in combination with GPs, has a limited sensitivity resulting in the potential for incorrect exclusion of AF, and interpreting ECGs to verify the presence of AF in this circumstance is likely to require additional interpretation from a competent healthcare professional. (80) Given the sensitivities of ECG diagnosis of AF in primary care were sufficiently low to give rise to substantial false negative cases of AF, it is conceivable that the skills of healthcare professionals in this setting would need improving to ensure the effectiveness of screening is not undermined. It would, however, be important to understand the current practise, skills and learning needs of primary care healthcare professionals before delivering any intervention to improve their abilities of accurately interpreting ECGs.

The third study (chapter six) - a survey of healthcare professionals in primary care – was the first study that engaged GP and nurse

stakeholders about AF screening and. The survey ascertained data for the feasibility of implementing AF screening in General Practices and the views of healthcare professionals in primary care about screening. The survey found that screening could be feasibly implemented within primary care as GP practices had the facilities to conduct and interpret ECGs as part of routine practice.

Screening for AF in primary care would result in a substantial increase in the number of ECGs conducted and that require interpretation. The findings from the survey suggest that non-GP healthcare professionals could have an important role in this. Although non-GP healthcare professionals reported more deficiencies in knowledge for ECG interpretation than GPs, they felt they would like to receive ECG training specifically for AF diagnosis. Furthermore, training to interpret ECGs and manage AF was identified as a facilitator for screening across all healthcare professional groups. Nurses may have the greatest potential for supporting AF screening. Nurses are having a greater role in managing long-term conditions, and research suggests that nurses prefer increased healthcare responsibilities, having an important role in disease management. (214, 215) Studies have also found that, with appropriate training, the accuracy of ECG interpretation by nurses can be improved. (216, 217)

Paradoxically, in the survey nurses reported they would not have a future role in AF diagnosis and management despite reporting they would like to receive ECG interpretation training. This may be due to nurses sometimes seeing their role in clinical practice as vague. (218) A number of barriers to AF screening were also identified, particularly relating to lack of workforce and capacity to undertake screening, which may influence nurses' lack of perceived role in future service delivery. The barriers to AF screening that the survey identified included lack of capacity, time, staff and funding to undertake screening activities within practices. Similar themes have been identified in studies investigating the introduction of screening for other conditions within primary care. (219-221) Furthermore, primary care in the UK is currently perceived to be in crisis, with surgeries facing cuts in funding, (222-224) poor recruitment, (225) and reduced job satisfaction reported by GPs. (222, 226) Any future AF screening programme would have financial and staffing implications to GP surgeries and overcoming these barriers, in addition to the facilitation of ECG interpretation training, would be imperative to ensure the successful implementation of this intervention.

7.2. Recommendations

7.2.1. Recommendations for clinical practice

Recommendation one: *In the first stage of screening for AF, newer technologies, such as modified blood pressure monitors and non-12-lead ECGs, could be used as alternatives to pulse palpation to detect pulse irregularities which may be caused by AF.*

As newer technologies were found to be more accurate than pulse palpation for detecting suspected AF using these technologies in AF detection is likely to be appropriate. New technologies could therefore be used for the first-step of AF screening if it were implemented.

Recommendation two: *In any screening programme, automated software analysis of 12-lead ECGs could be used to support healthcare professionals identify normal ECGs and also to rule in the presence of AF.*

Automated software analysis of 12-lead ECGs was found to have a greater specificity for AF diagnosis than other methods of ECG interpretation. This would result in those without AF being correctly identified alongside a low false positive rate of AF diagnoses. Therefore, a positive test result when diagnosing AF using automated ECG interpretation, in the context of a high specificity,

215

would also support healthcare professionals ruling in the presence of AF. However, the sensitivity of automated software analysis was not sufficiently high for this method to be reliably used in isolation to rule out AF, as the lower sensitivity would result in a high rate of false negative diagnoses of AF.

Recommendation three: *In a screening programme, practice nurses could be used to detect pulse irregularities caused by AF (the first-step of screening) and GPs could be used to interpret ECGs (the second-step of screening).*

Practice nurses were found to have confidence in undertaking AF screening activities, such as pulse palpation and performing 12-lead ECGs, more often than GPs. Therefore, they could have a role in the first-step of AF screening where patients with an irregular pulse are identified. Of primary care professionals, GPs were found to have a greater confidence and accuracy for interpreting ECGs and diagnosing AF than nurses; GPs are therefore the most likely professional group to undertake the second-step of screening in primary care. However, it is likely that training would be required for GPs to ensure competencies in ECG interpretation are achieved.

7.2.2. Recommendations for research

Recommendation 1: *Studies of AF screening are required that compare the effectiveness and cost-effectiveness of newer technologies, such a modified blood pressure monitors and non-12-lead ECGs, to pulse palpation for the detection of AF*

Although newer technologies were found to have a greater accuracy than pulse palpation for detecting suspected AF, there have been no studies comparing the effectiveness and cost-effectiveness of such technologies to pulse palpation for detecting silent AF. Economic analyses should consider the greater yield of AF detection using new technologies and how this could offset the greater cost of implementing these into routine practice. This research would improve the understanding of how the recommended first-step of AF screening could be optimized.

Recommendation 2: *Studies are required that investigate improving the competencies of healthcare professionals in primary care to interpret 12-lead ECGs for the diagnosis of AF*

The accuracy of diagnosing AF using ECGs in primary care is likely to require improvement before screening could be implemented. This would be particularly important if nurses were to have a role in future AF screening; practice nurses perceived to have less

confidence, knowledge and skills than GPs to competently interpret ECGs and diagnose AF, and extending their role to undertake this is likely to require further training. Consequently, studies investigating methods of improving the abilities of GPs and/or nurses for interpreting 12-lead-ECGs are an important priority. This may include research that investigates combining healthcare professional and software ECG interpretation as automated software was found to have the greatest accuracy for determining normal ECGs. An important consideration when designing such research would be to ensure a high internal and external validity. The second systematic review undertaken in this thesis (chapter 5) found study quality – as assessed using the QUADAS-2 tool – was generally low. The QUADAS-2 tool could be used to inform the development of diagnostic accuracy studies to ensure the design, conduct and reporting of future research is of a high standard and translatable to different healthcare settings.

Although many ECG training courses are available, to my knowledge there has been no systematic evaluation of the effectiveness of ECG training programmes to improve the accuracy of ECG interpretation by healthcare professionals in primary care. Indeed, such research would subsequently help inform how ECG interpretation and AF diagnosis could be quality assured as part of screening.

Recommendation 3: *Studies are required that investigate the views of healthcare professionals in primary care from non-inner city and rural areas, and other key stakeholders, about AF screening*

The survey suggested it may be feasible to introduce screening within primary care and that healthcare professionals were enthusiastic about potential screening implementation. However, the generalisability of these findings would require testing in other practice settings. The survey also investigated healthcare professionals' perceived knowledge and skills about AF screening and further research that objectively quantifies existing knowledge and skills would enable validation of the survey findings.

Qualitative research would provide greater understanding of the views expressed by healthcare professionals in the survey about screening implementation. Although the survey used open-ended questions to help identify facilitators and barriers to screening, qualitative research methods would enable in-depth understanding of the themes identified.

Furthermore, there has been a paucity of research investigating the views of other key healthcare professional groups such as Public Health England, NHS England and Clinical Commissioning Groups, and understanding the views of these stakeholders would

inform the development and implementation of future AF screening.

Other stakeholders in AF screening are the service users. Although the literature review (chapter 2) identified some research about patient views of AF screening, there is little data on informed choice about AF screening. Such research would a provide greater understanding about the factors associated with patient engagement in AF screening programmes and help overcome patient related barriers to implementation.

Recommendation 4: *Studies are required that investigate long-term clinical outcomes in patients with screen-detected AF*

The literature review from chapter two found only one study that reported clinical outcomes, other than new cases of AF, in those with screen-detected AF. Currently, AF screening studies report the stroke risk scores of people with screen-detected AF at the point of detection. However, there are no studies that report the subsequent change in long-term stroke burden as a consequence of treating those with screen-detected AF. As screening aims to reduce the thromboembolic complications arising from silent AF, research that compares treatment provision and longer-term clinical outcomes, such as changes in stroke burden and

complications from the treatment, in those with screen-detected AF and those with AF detected from routine practice would be required.

Recommendation 5: *Studies are required that compare the effectiveness, cost-effectiveness and affordability of AF screening methods to usual care*

A finding from the literature review undertaken in chapter two was that there was a paucity of studies comparing the effectiveness of screening methods to usual care. Most studies of AF screening have been uncontrolled case finding studies and suggest silent AF exists and that it can be detected. Randomised trials of AF screening found screening, using pulse palpation and/or 12-lead ECG, to be more effective than usual practice at detecting new cases of AF. As newer technologies are increasingly used to detect pulse irregularities caused by AF, randomised trial evidence is required that compares the effectiveness and cost-effectiveness of AF detection using such methods to AF detection that would arise from routine practice. Moreover, economic analyses that model the subsequent affordability and opportunity costs of screening if delivered at a population level would help inform the equitable delivery of healthcare services.

Recommendation six: Studies are required that investigate the effectiveness, cost effectiveness and subsequent affordability of AF screening in different target populations according to age

Screening for AF has been recommended in patient's ≥65 years of age. Although the literature review in chapter two found that most studies of AF screening included people ≥65 years, there were no studies that investigated the effectiveness and cost-effectiveness of screening by varying the age thresholds of inclusion. The prevalence of AF and the risk of stroke attributable to AF increase with age; it is therefore possible that screening could be more effective and cost-effective if the age threshold of including participants for screening is increased, and research investigating the impact of varying age thresholds would inform how screening could be optimally organised.

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Appendices

Appendix 1: Chapter 4 - Electronic search strategy

Medline (1946 to March Week 2 2015) - search completed:

16/03/2015

Disease

1)   Atrial fibrillation – MESH - 27734

2)   Atrial fibrillation.mp - 35999

3)   Auricular fibrillation*.mp - 76

4)   Atrium fibrillation*.mp - 7

5)   Af.mp - 21099

6)   A-fib.mp – 38

7)   Atrial flutter – MESH - 2598

8)   Atrial flutter*.mp - 3593

9)   Auricular flutter*.mp - 6

10)   Irregular pulse.mp – 36

11)   Irregular pulse*.mp - 48

12)   Irregular heart*.mp - 123

13)   Heart beat*.mp - 2416

14)   Irregular rhythm*.mp – 84

Screening

15)   Screen*.mp - 380961

16)   Diagnostic procedure.mp – 3307

17) Diagnosis – MESH - 3858748

18) Diagnos*.mp - 1234132

19) Identif*.mp - 1480379

20) Test*.mp - 1778554

21) Detect*.mp – 1099413

Device

22) Electrocardiography – MESH - 72662

23) Electrocardiogram*.mp - 19087

24) Electrocardiograph*.mp - 76279

25) Blood pressure monitors –MESH – 940

26) Blood pressure monitor*.mp - 8977

27) Blood pressure device*.mp - 142

28) Ecg.mp - 27825

29) Ekg.mp - 1339

30) Holter.mp - 4738

31) Event monitor*.mp - 638

32) Pulse adj3 test*.mp - 682

33) Pulse palpation.mp – 61

34) Device*.mp - 182533

35) Watch BP home A.mp – 0

Professionals

36) Physicians – MESH - 51096

37) Doctor*.mp – 58183

38) Nurses – MESH - 42126

39) Nurse*.mp – 166128

40) Health personnel – MESH - 224026

41) Healthcare worker*.mp - 4164

42) Healthcare professional*.mp - 7882

43) Primary Health Care – MESH - 63601

44) Secondary Care – MESH - 137

45) Hospitals – MESH - 105602

46) General Practice- MESH – 36745

Testing

47) Accuracy.mp - 165781

48) Sensitivity and Specificity – MESH – 387754

49) Sensitivity.mp - 588915

50) Specificity.mp – 564148

51) Predictive value of tests- MESH – 129242

52) Positive predictive value*.mp - 24040

53) Negative predictive value*.mp – 24214

Combining "OR" searches

54) 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or
13 or 14 – 49725

55) 15 or 16 or 17 or 18 or 19 or 20 or 21 – 6274796

56) 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 – 280651

57) 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 – 520477

58) 47 or 48 or 49 or 50 or 51 or 52 or 53 – 1057202

59) 55 or 56 – 6340796

Combination "AND" searches

60) 54 and 57 and 58 and 59 – 83

61) 54 and 58 and 59 – 4518

62) Limit 60 to humans and all adults aged 19 plus – 63

63) Limit 61 to humans and all adults aged 19 plus - 3194

Embase (1980 to Week 11 2015) - searched completed: 16/03/2015

Disease

1) Atrial fibrillation – MESH - 87943

2) Atrial fibrillation.mp - 69156

3) Auricular fibrillation*.mp - 922

4) Atrium fibrillation*.mp - 87943

5) Af.mp - 52764

6) A-fib.mp – 162

7) Atrial flutter – MESH - 9625

8) Atrial flutter*.mp - 6648

9) Auricular flutter*.mp - 249

10) Irregular pulse*.mp - 143

11) Irregular heart*.mp - 332

12) Heart beat*.mp - 9041

13) Irregular rhythm*.mp – 227

Screening

14) Screen*.mp - 861041

15) Diagnostic procedure - MESH – 12700923

16) Diagnostic procedur*.mp – 92698

17) Diagnosis – MESH - 4973477

18) Diagnos*.mp - 3566708

19) Identif*.mp - 2629324

20) Test*.mp - 3521441

21) Detect*.mp – 2120135

Device

22) Electrocardiography – MESH - 156369

23) Electrocardiogram*.mp - 111191

24) Electrocardiograph*.mp - 161434

25) Blood pressure monitors –MESH – 543

26) Blood pressure monitor*.mp - 26211

27) Blood pressure device*.mp - 286

28) Ecg.mp - 79109

29) Ekg.mp - 7772

30) Holter.mp - 17288

31) Event monitor*.mp - 1242

32) Pulse adj3 test*.mp - 1530

33) Pulse palpation.mp – 142

34) Device*.mp - 419080

35) Watch BP home A.mp – 0

Professionals

36) Physician – MESH - 440074

37) Doctor*.mp – 198770

38) Nurse – MESH - 120534

39) Nurse*.mp – 315282

40) Health personnel – MESH - 988237

41) Healthcare worker*.mp - 6651

42) Healthcare professional*.mp - 14208

43) Primary Health Care – MESH - 113103

44) Secondary health Care – MESH - 1793

45) Hospital – MESH - 749092

46) General Practice- MESH – 70966

Testing

47) Accuracy.mp - 524616

48) Sensitivity and Specificity – MESH – 217170

49) Sensitivity.mp - 970195

50) Specificity.mp – 630639

51) Predictive value - MESH – 66593

52) Positive predictive value*.mp - 40792

53) Negative predictive value*.mp – 41030

Combining "OR" searches

54) 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or – 135741

55) 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 – 15473280

56) 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 – 707833

57) 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 – 1928353

58) 47 or 48 or 49 or 50 or 51 or 52 or 53 – 1689943

59) 55 or 56 - 15623672

Combination "AND" searches

60) 54 and 57 and 58 and 59 – 842

61) 54 and 58 and 59 – 8285

62) Limit 60 to humans and all adult (<18 to 64 years) – 179

63) Limit 60 to humans and all aged (<65+ years) – 195

64) 62 or 63 - 263

65) Limit 61 to humans and all adult (<18 to 64 years) – 2620

66) Limit 61 to humans and all aged (<65+ years) - 2234

67) 65 or 66 - 3344

CINAHL - search completed: 16/03/2015

Disease

((MM "Atrial Fibrillation") OR "atrial fibrillation" OR (MH "Atrial Flutter")) OR auricular fibrillation OR atrium fibrillation OR af OR a-fib OR auricular flutter OR irregular pulse OR irregular heart OR irregular rhythm OR heart beat

Above found 17,541 results

Screening

((MM "Diagnosis+") OR "diagnosis" OR (MM "Diagnosis, Cardiovascular+") OR (MM "Diagnosis, Computer Assisted+")) OR screen OR identify OR test OR detect OR procedure
Above found 1,090,817

Device

((MM "Electrocardiography+") OR "electrocardiography" OR (MM "Electrocardiography, Ambulatory") OR (MM "Cardiography, Impedance")) OR electrocardiogram OR blood pressure monitor

OR blood pressure device OR ecg OR ekg OR holter OR event monitor OR pulse adj3 test OR pulse palpation OR device OR watch BP home A

Above found 57,950

Professionals

((MM "Physicians+") OR "physicians") OR doctor OR nurse OR health personnel OR healthcare worker OR healthcare professional OR primary health care OR secondary care OR hospital OR general practice

Above found 496,183

Testing

((MM "Sensitivity and Specificity") OR "sensitivity") OR accuracy OR specificity OR predictive value of test OR positive predictive value OR negative predictive value

Above found 116,781

Combination "AND" searches

1)   1 AND 2 AND 3 AND 4 AND 5 – 24

2)   1 AND 5 AND 6 – 638

((atrial fibrillation*) OR (auricular fibrillation*) OR (Atrium fibrillation*) OR (AF) OR (A-fib) OR (Atrial flutter*) OR (Auricular flutter*) OR (irregular pulse*) OR (irregular heart*) OR (heart beat*) OR (irregular rhythm)) AND ((Accuracy*) OR (sensitivity) OR (specificity) OR (predictive value of test*) OR (positive predictive value*) OR (negative predictive value*)) AND (((((Screen*) OR (diagnostic procedure) OR (diagnos*) OR (identif*) OR (test*) OR (detect*)) OR ((electrocardiograph*) OR (electrocardiogram*) OR (blood pressure monitor*) OR (blood pressure device*) OR (ecg) OR (ekg) OR (holter) OR (event monitor*) OR (pulse adj3 test*) OR (pulse palpation) OR (device*) OR (watch BP home A)))) AND (db:("LILACS")) = 61

Appendix 2: Chapter 4 - Data extraction table

Category	Data extracted
Basic Study characteristics	Author
	Year
	Title/question
	Design
	Years of enrolment
	Country of origin
	Funding source
Participant's characteristics	Brief description of participants
	Inclusion criteria
	Exclusion criteria
	Baseline characteristics of participants
	Number of potential participants
	Number of participants who refused
	Number recruited
	Number lost to follow up/drop out
	Reasons for loss to follow up/drop out
Comparator Intervention	Device
	Manufacturer
	Diagnostic method and interpretation
	Threshold value

	Other information
Experimental Intervention	Device
	Manufacturer
	Diagnostic method and interpretation
	Threshold value
	Other information
Other information	Length of time between experimental intervention and comparator
Results	Sample size (if different to initial numbers)
	True positive
	False positive
	False negative
	True negative
	Sensitivity
	Specificity
	Positive predictive value
	Negative predictive value

Appendix 3: Chapter 5 - Electronic search strategy

Medline (1946 to March Week 3 2014) - search completed:

24/03/2014

Disease

1)   (Heart) atrial fibrillation – MESH - 32301

2)   Atrial fibrillation.mp - 41749

3)   Auricular fibrillation*.mp - 1283

4)   Atrium fibrillation*.mp - 7

5)   Af.mp - 32254

6)   A-fib.mp – 36

7)   Atrial flutter – MESH - 4887

8)   Atrial flutter*.mp - 6326

9)   Auricular flutter*.mp - 410

10)   Irregular pulse.mp – 55

11)   Irregular pulse*.mp - 71

12)   Irregular heart*.mp - 155

13)   Heart beat*.mp - 3438

14)   Irregular rhythm*.mp – 132

Screening

15)   Screen*.mp - 462367

16)   Diagnostic procedure.mp – 5624

17)   Diagnosis – MESH - 6340318

18)   Diagnos*.mp - 1845810

19) Identif*.mp - 1735408

20) Test*.mp - 2643310

21) Detect*.mp – 1479266

Device

22) Electrocardiography – MESH - 172776

23) Electrocardiogram*.mp - 31874

24) Electrocardiograph*.mp - 178114

25) Blood pressure monitors –MESH – 1926

26) Blood pressure monitor*.mp - 10505

27) Blood pressure device*.mp - 199

28) Ecg.mp - 43840

29) Ekg.mp - 4459

30) Holter.mp - 7862

31) Event monitor*.mp - 708

32) Pulse adj3 test*.mp - 1127

33) Pulse palpation.mp – 82

34) Device*.mp - 226332

35) Watch BP home A.mp – 0

Professionals

36) Physicians – MESH - 83260

37) Doctor*.mp – 81292

38) Nurses – MESH - 68290

39) Nurse*.mp – 253375

40) Health personnel – MESH - 357173

41) Healthcare worker*.mp - 3968

42) Healthcare professional*.mp - 7001

43) Primary Health Care – MESH - 75611

44) Secondary Care – MESH - 43

45) Hospitals – MESH - 194688

46) General Practice- MESH – 62966

Testing

47) Accuracy.mp - 192073

48) Sensitivity and Specificity – MESH – 400650

49) Sensitivity.mp - 743377

50) Specificity.mp – 793646

51) Predictive value of tests- MESH – 136172

52) Positive predictive value*.mp - 25647

53) Negative predictive value*.mp – 24978

Combining "OR" searches

54) 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 – 70362

55) 15 or 16 or 17 or 18 or 19 or 20 or 21 – 9651773

56) 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 – 436716

57) 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 – 826469

58) 47 or 48 or 49 or 50 or 51 or 52 or 53 – 1429831

59) 55 or 56 – 9750420

Combination "AND" searches

60) 54 and 57 and 58 and 59 – 75

61) 54 and 58 and 59 – 4475

62) Limit 60 to humans and all adults aged 19 plus – 52

63) Limit 61 to humans and all adults aged 19 plus - 2976

After removing duplicates, these reduced to:

62) 52 citations

63) 2790 citations

Embase (1980 to Week 22 2013) - searched completed: 24/03/2014

Disease

1) (Heart) atrial fibrillation – MESH - 69630

2) Atrial fibrillation.mp - 54189

3) Auricular fibrillation*.mp - 884

4) Atrium fibrillation*.mp - 69636

5) Af.mp - 45907

6) A-fib.mp – 98

7) Atrial flutter – MESH - 8403

8) Atrial flutter*.mp - 5836

9) Auricular flutter*.mp - 242

10) Irregular pulse*.mp - 107

11) Irregular heart*.mp - 247

12) Heart beat*.mp - 7869

13) Irregular rhythm*.mp – 176

Screening

14) Screen*.mp - 725649

15) Diagnostic procedure - MESH – 11093533

16) Diagnostic procedur*.mp – 85626

17) Diagnosis – MESH - 4230862

18) Diagnos*.mp - 2997012

19) Identif*.mp - 2207650

20) Test*.mp - 3018483

21) Detect*.mp – 1845302

Device

22) Electrocardiography – MESH - 141891

23) Electrocardiogram*.mp - 93464

24) Electrocardiograph*.mp - 146198

25) Blood pressure monitors –MESH – 109

26) Blood pressure monitor*.mp - 23151

27) Blood pressure device*.mp - 260

28) Ecg.mp - 65822

29) Ekg.mp - 6484

30) Holter.mp - 15340

31) Event monitor*.mp - 1052

32) Pulse adj3 test*.mp - 1375

33) Pulse palpation.mp – 107

34) Device*.mp - 334361

35) Watch BP home A.mp – 0

Professionals

36) Physician – MESH - 325066

37) Doctor*.mp – 176308

38) Nurse – MESH - 100677

39) Nurse*.mp – 277825

40) Health personnel – MESH - 802719

41) Healthcare worker*.mp - 5398

42) Healthcare professional*.mp - 10331

43) Primary Health Care – MESH - 98105

44) Secondary health Care – MESH - 291

45) Hospital – MESH - 585982

46)   General Practice- MESH – 66974

Testing

47)   Accuracy.mp - 444114

48)   Sensitivity and Specificity – MESH – 191084

49)   Sensitivity.mp - 837582

50)   Specificity.mp – 570265

51)   Predictive value - MESH – 34084

52)   Positive predictive value*.mp - 34537

53)   Negative predictive value*.mp – 34398

Combining "OR" searches

54)   1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or – 115107

55)   14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 – 13550282

56)   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 – 590094

57)   36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 – 1596142

58)   47 or 48 or 49 or 50 or 51 or 52 or 53 – 1466660

59)   55 or 56 - 13677296

Combination "AND" searches

60)   54 and 57 and 58 and 59 –551

61) 54 and 58 and 59 – 6289

62) Limit 60 to humans and all adult (<18 to 64 years) – 128

63) Limit 60 to humans and all aged (<65+ years) – 134

64) 62 or 63 - 179

65) Limit 61 to humans and all adult (<18 to 64 years) – 2134

66) Limit 61 to humans and all aged (<65+ years) - 1806

67) 65 or 66 - 2646

After removing duplicates, these reduced to:

64) 116 citations

67) 1362 citations

CINAHL - search completed: 24/04/2014

Disease

((MM "Atrial Fibrillation") OR "atrial fibrillation" OR (MH "Atrial Flutter")) OR auricular fibrillation OR atrium fibrillation OR af OR a-fib OR auricular flutter OR irregular pulse OR irregular heart OR irregular rhythm OR heart beat

Above found 14,250 results

Screening

((MM "Diagnosis+") OR "diagnosis" OR (MM "Diagnosis, Cardiovascular+") OR (MM "Diagnosis, Computer Assisted+")) OR screen OR identify OR test OR detect OR procedure

Above found 917,175

Device

((MM "Electrocardiography+") OR "electrocardiography" OR (MM "Electrocardiography, Ambulatory") OR (MM "Cardiography, Impedance")) OR electrocardiogram OR blood pressure monitor OR blood pressure device OR ecg OR ekg OR holter OR event monitor OR pulse adj3 test OR pulse palpation OR device OR watch BP home A

Above found 49,451

Professionals

((MM "Physicians+") OR "physicians") OR doctor OR nurse OR health personnel OR healthcare worker OR healthcare professional OR primary health care OR secondary care OR hospital OR general practice

Above found 451,595

Testing

((MM "Sensitivity and Specificity") OR "sensitivity") OR accucracy OR specificity OR predictive value of test OR positive predictive value OR negative predictive value

Above found 81,595

Combining "OR" Searches

Screening + Device – 936,310

Combination "AND" searches

64)   1 AND AND 4 AND 5 AND 6 – 40

65)   1 AND 5 AND 6 – 468

Restricting for adult gives:

1) 25

2) 344

After removing duplicates, the CINAHL search returned:

1)   5

2)   38

LILACS - search completed:24/03/2014

((atrial fibrillation*) OR (auricular fibrillation*) OR (Atrium fibrillation*) OR (AF) OR (A-fib) OR (Atrial flutter*) OR (Auricular flutter*) OR (irregular pulse*) OR (irregular heart*) OR (heart beat*) OR (irregular rhythm)) AND ((Physician*) OR (Doctor*) OR (Nurse*) OR (health personnel) OR (healthcare worker*) OR (health care professional*) OR (primary health care) OR (secondary care OR hospital*) OR (general practice*)) AND ((Accuracy*) OR (sensitivity) OR (specificity) OR (predictive value of test*) OR (positive predictive value*) OR (negative predictive value*)) AND ((

((Screen*) OR (diagnostic procedure) OR (diagnos*) OR (identif*) OR (test*) OR (detect*)) OR ((electrocardiograph*) OR (electrocardiogram*) OR (blood pressure monitor*) OR (blood pressure device*) OR (ecg) OR (ekg) OR (holter) OR (event monitor*) OR (pulse adj3 test*) OR (pulse palpation) OR (device*) OR (watch BP home A)))) AND (db:("LILACS")) = 3

((atrial fibrillation*) OR (auricular fibrillation*) OR (Atrium fibrillation*) OR (AF) OR (A-fib) OR (Atrial flutter*) OR (Auricular flutter*) OR (irregular pulse*) OR (irregular heart*) OR (heart beat*) OR (irregular rhythm)) AND ((Accuracy*) OR (sensitivity) OR (specificity) OR (predictive value of test*) OR (positive predictive value*) OR (negative predictive value*)) AND (((((Screen*) OR (diagnostic procedure) OR (diagnos*) OR

(identif*) OR (test*) OR (detect*)) OR ((electrocardiograph*) OR (electrocardiogram*) OR (blood pressure monitor*) OR (blood pressure device*) OR (ecg) OR (ekg) OR (holter) OR (event monitor*) OR (pulse adj3 test*) OR (pulse palpation) OR (device*) OR (watch BP home A)))) AND (db:("LILACS")) = 20

After removing duplicates compared to Medline and Embase, search 1 returns 3, search 2 returns 16.

Appendix 4: Chapter 6 - Healthcare professional survey

ID CODE (*for research team use only*):

Your views on detecting and diagnosing atrial fibrillation (AF) in primary care

Please complete the following questionnaire by ticking the boxes that are most appropriate to you or by writing in the spaces provided. All information given is confidential. Unless stated, please only tick one box per question.

SECTION 1: About you

1. Are you a:

    General practitioner ☐

    Nurse practitioner ☐

    Nurse ☐

    Healthcare assistant ☐

2. How many years have you been practising as a healthcare professional (**nearest whole years**)?

    ----

3. Do you currently work full time in general practice?

    Yes ☐ ➡ **SKIP TO QUESTION 5**   No ☐

4. If part time, how many **days** do you work in a normal week?   ------------------------

PLEASE TURN OVER

SECTION 2: About your current practice

5.   Do you perform pulse checks to identify if a patient has an irregular pulse?

Yes ☐   No ☐ ➡ **SKIP TO QUESTION 7**

6.   How often do you perform pulse checks to identify an irregular pulse?

Always   ☐

Often   ☐

Sometimes ☐

Rarely   ☐

7.   Does your GP surgery have a 12-lead ECG machine?

Yes ☐   No ☐ ➡ **SKIP TO QUESTION 15**

8.   Who carries out the 12-lead ECG on patients to obtain a heart tracing at your practice (*tick all those which are applicable*)?

General practitioner ☐

Nurse practitioner   ☐

Nurse   ☐

Healthcare assistant ☐

Other (**please specify**): ....

9.   Is the decision about whether a 12-lead ECG shows AF made within your practice?

Yes ☐   No ☐ ➡ **SKIP TO QUESTION 14**

10.   If yes, how often is this decision made at your practice:

Always   ☐ ➡ **SKIP TO QUESTION 13**

Often   ☐

Sometimes ☐

Rarely   ☐

Don't know ☐

PLEASE TURN OVER

Screening for AF in primary care: Page **2** of **10**

12.   Where else is the decision about whether a 12-lead ECG shows AF made (*tick all those which are applicable*)?

Another NHS GP practice   ☐

NHS hospital   ☐

Private health care provider ☐

Other (**please specify**):⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯

Don't know   ☐

13.   Which health professional at your practice usually makes the decision about whether a 12-lead ECG shows AF (*tick all those which are applicable*)?

General practitioner   ☐

Nurse practitioner   ☐

Nurse   ☐

Healthcare assistant   ☐

Other (**please specify**):⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯

Don't know   ☐

PLEASE SKIP TO QUESTION 21

14.   If no, where is the decision about whether a 12-lead ECG shows AF made (*tick all those which are applicable*)?

Another NHS GP practice   ☐

NHS hospital   ☐

Private health care provider ☐

Other (**please specify**):⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯⎯

Don't know   ☐

PLEASE SKIP TO QUESTION 21

PLEASE TURN OVER

15. If you DON'T have a 12-lead ECG machine at your practice, how do you obtain a 12-lead ECG on your patients (*tick all those which are applicable*)?

Another NHS GP practice ☐

NHS hospital ☐

Private health care provider ☐

Other (**please specify**):_____

Don't know ☐

16. Is the decision about whether a 12-lead ECG shows AF made within your practice?

Yes ☐ No ☐ ➡ **SKIP TO QUESTION 20**

17. If yes, how often is the decision about whether a 12-lead ECG shows AF made at your practice:

Always ☐ ➡ **SKIP TO QUESTION 19**

Often ☐

Sometimes ☐

Rarely ☐

Don't know ☐

18. Where else is the decision about whether a 12-lead ECG shows AF made (*tick all those which are applicable*)?

Another NHS GP practice ☐

NHS hospital ☐

Private health care provider ☐

Other (**please specify**):_____

Don't know ☐

19. At your practice, which health professional usually makes the decision about whether a 12-lead ECG shows AF (*tick all those which are applicable*)?

General practitioner ☐

Nurse practitioner ☐

Nurse ☐

Healthcare assistant ☐

Other (please specify):_____

Don't know ☐

PLEASE SKIP TO QUESTION 21

20.   If no, where is the decision about whether an 12-lead ECG shows AF made (*tick all those which are applicable*)?

Another NHS GP practice ☐

NHS hospital ☐

Private health care provider ☐

Other (**please specify**): ┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄┄

Don't know ☐

PLEASE TURN OVER

SECTION 3: Your thoughts on training for diagnosing AF

21.   Since you have graduated/become a healthcare professional have you received any additional training about how to interpret 12-lead ECGs?

Yes ☐   No ☐ ➡ **SKIP TO QUESTION 23**

22.   How long ago did you receive this?

Less than one year ago   ☐
Between one and five years ago ☐
More than five years ago   ☐

23.   How confident do you feel in performing the following tasks? (*Tick **one** box only for each question*)

	Very confident	Somewhat confident	Not confident at all
Identifying an irregular pulse using pulse palpation	☐	☐	☐
Performing a 12-lead ECG	☐	☐	☐
Deciding if a 12-lead ECG shows AF	☐	☐	☐

PLEASE TURN OVER

24.   How would you rate your knowledge about the following tasks? (*Tick **one** box only for each question*)

	Excellent	Good	Fair	Poor	Non-existent
Identifying patients with an irregular pulse	☐	☐	☐	☐	☐
Deciding about the cause of an abnormal 12-lead ECG	☐	☐	☐	☐	☐
Deciding if a 12-lead ECG shows AF	☐	☐	☐	☐	☐
Deciding on the treatment of AF once it has been diagnosed	☐	☐	☐	☐	☐

PLEASE TURN OVER

25.   We're interested in how you feel about atrial fibrillation. Below are a series of statements on this subject.

*Please tick **one** box for your most appropriate response to each statement*

	Strongly agree	Agree	Not sure	Disagree	Strongly disagree
I would benefit from further training on how to identify an irregular pulse in patients	☐	☐	☐	☐	☐
I would benefit from further training about how to interpret a 12-lead ECG for any condition	☐	☐	☐	☐	☐
I would benefit from further training about how to decide if a 12-lead ECG shows AF	☐	☐	☐	☐	☐
I would be better at diagnosing AF if I received training about how to interpret a 12-lead ECG	☐	☐	☐	☐	☐
I would like to receive training on how to interpret a 12-lead ECG for any condition	☐	☐	☐	☐	☐
I would like to receive training on how to decide if a 12-lead ECG shows AF	☐	☐	☐	☐	☐
I would like to be involved in diagnosing patients with AF	☐	☐	☐	☐	☐

26.   Are there any specific areas about the diagnosis of AF using 12-lead ECGs that you would like training?

PLEASE TURN OVER

SECTION 4: Your thoughts on screening for AF

It has been suggested that screening for AF in primary care is a relatively effective and cost-effective way of identifying people with AF. Current guidelines suggest that screening should involve using pulse palpation to identify patients with an irregular pulse, and then a 12-lead ECG should be conducted to determine whether the irregular pulse is caused by AF.

27.   If your practice was compelled to take part in such a national screening program, what role could you see yourself having in this?

	Very likely	Likely	Unsure	Unlikely	Very unlikely
Conduct pulse checks to identify an irregular pulse	☐	☐	☐	☐	☐
Conduct 12-lead ECGs on patients with an irregular pulse	☐	☐	☐	☐	☐
Deciding if a 12-lead ECG shows AF	☐	☐	☐	☐	☐
Making the diagnosis of AF in a patient	☐	☐	☐	☐	☐

28.   If such a screening program was introduced, what further training would you need to be able to undertake this role?

----

29.   If a screening program for AF was introduced, are there any problems you think might prevent it working effectively at your surgery?

PLEASE TURN OVER

ID CODE (*for research team use only*):

30. Would you like to receive a summary of the survey results?

    Yes ☐   No ☐

31. Would you like to be contacted about participating in future research about AF?

    Yes ☐   No ☐

32. If yes, please leave your contact details below:

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

Appendix 5: Research outputs

Publications (peer reviewed)

Taggar JS, Coleman T, Lewis S, Heneghan C, Jones M. Accuracy of methods for detecting an irregular pulse and suspected atrial fibrillation: A systematic review and meta-analysis. Eur J Prev Cardiol. 2016;23(12):1330-8. doi: 10.1177/2047487315611347. [Original research – Chapter 4]

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. doi: 10.1016/j.ijcard.2015.02.014. [Original research – Chapter 5]

Taggar JS, Coleman T, Lewis S, Jones M. Screening for Atrial Fibrillation - A Cross-Sectional Survey of Healthcare Professionals in Primary Care. PLoS One. 2016;11(4):e0152086. doi: 10.1371/journal.pone.0152086 [Original research – Chapter 6]

Taggar JS, Coleman T. Screening for atrial fibrillation in primary care: From recommendation to implementation. Eur J Prev Cardiol. 2016;23(17):1880-1882 [Commentary]

Abstract presentations

Taggar J, Coleman T, Lewis S, Heneghan C, Jones M. Accuracy of methods for detecting Atrial Fibrillation: A systematic review. Society for Academic Primary Care Meeting. 9-11th July 2014, Edinburgh [Presentation]

Taggar J, Coleman T, Lewis S, Heneghan C, Jones M. Accuracy of methods for diagnosing Atrial Fibrillation: A systematic review. Society for Academic Primary Care Meeting. 9-11th July 2014, Edinburgh [Presentation]

Taggar JS, Coleman T, Lewis S, Jones M. Screening for Atrial Fibrillation - A Cross-Sectional Survey of Healthcare Professionals in Primary Care. Society for Academic Primary Care. Society for Academic Primary Care Annual Scientific Meeting. 6-8th July 2016, Dublin [Presentation]